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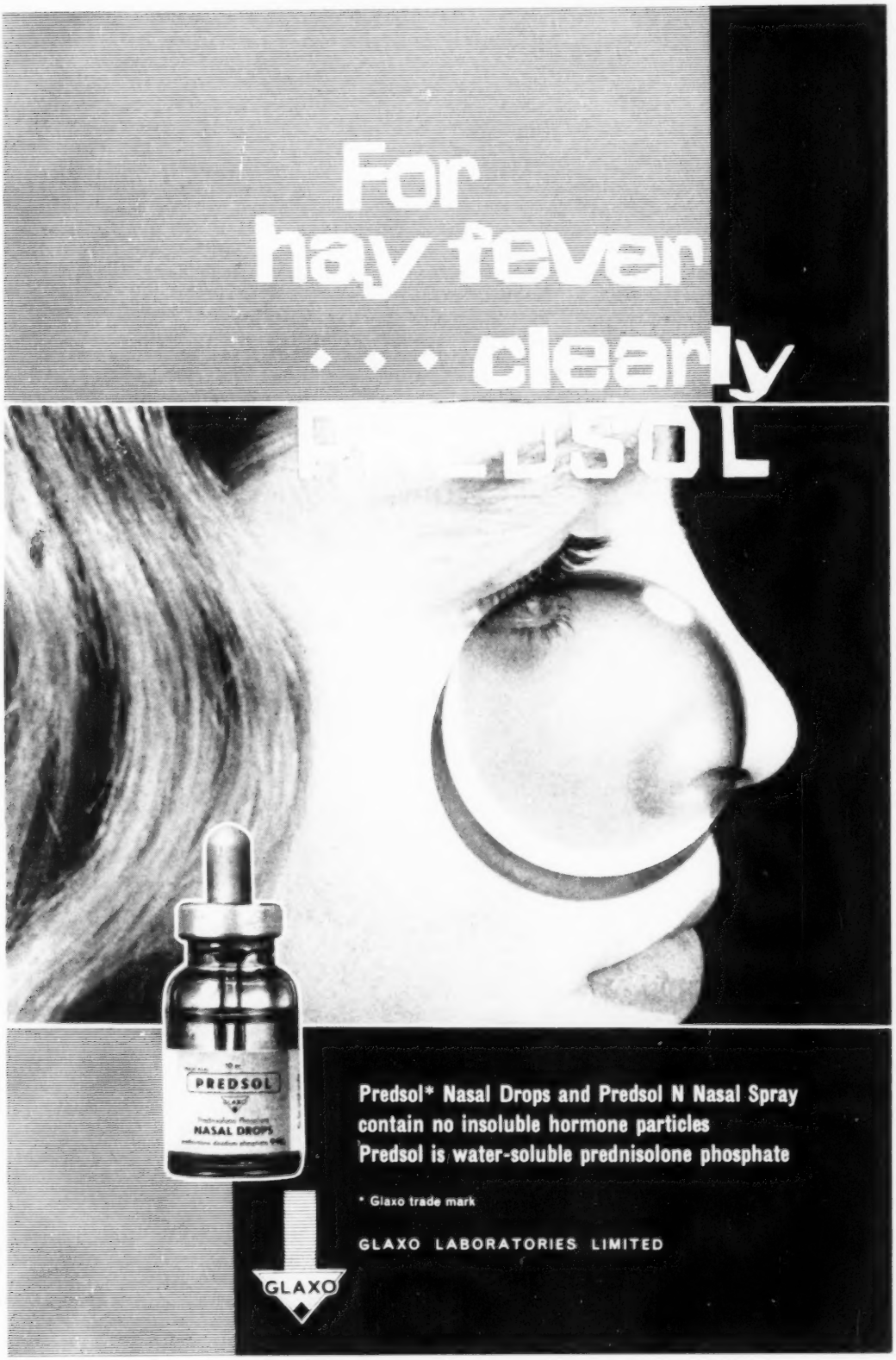
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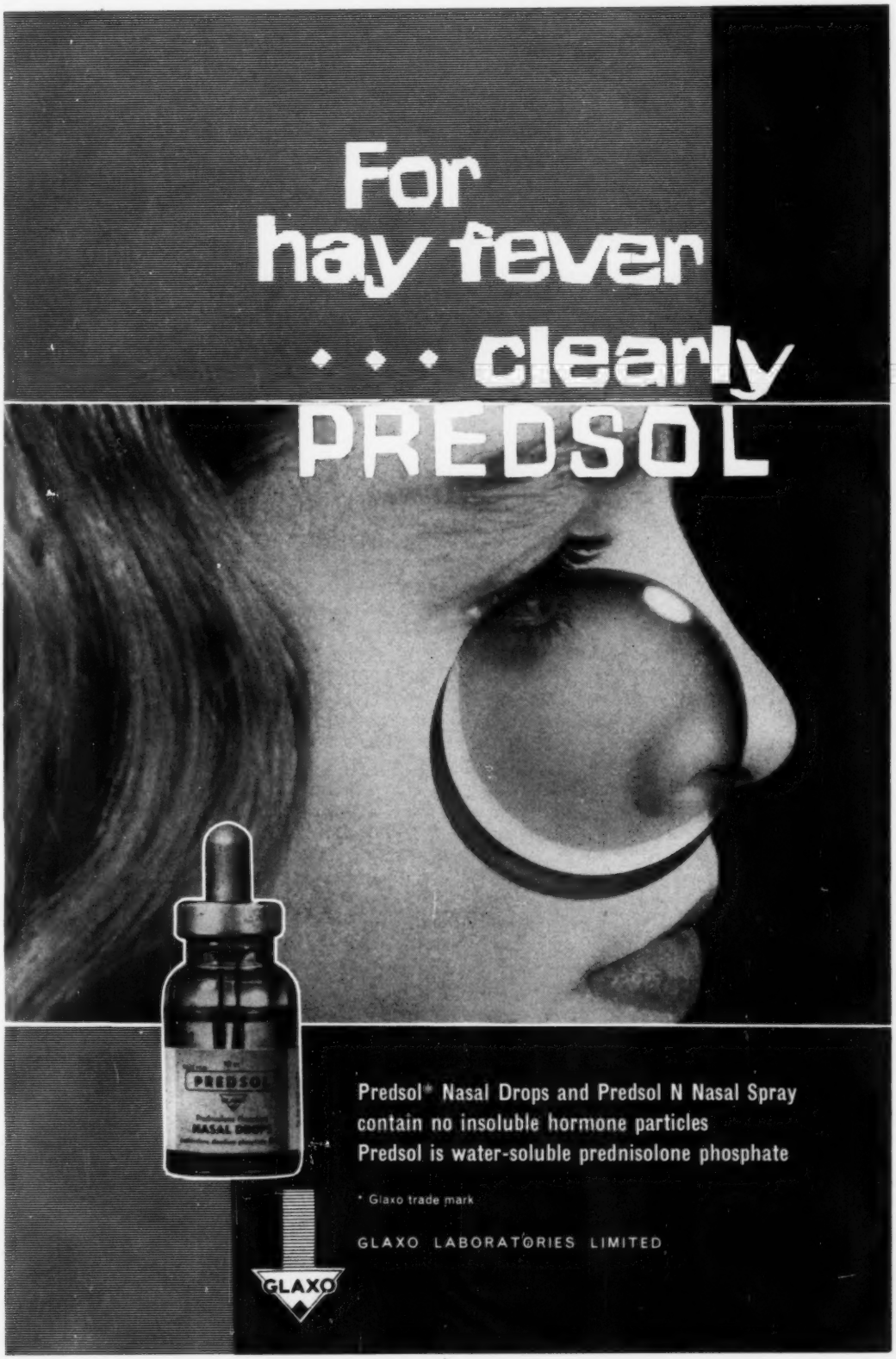
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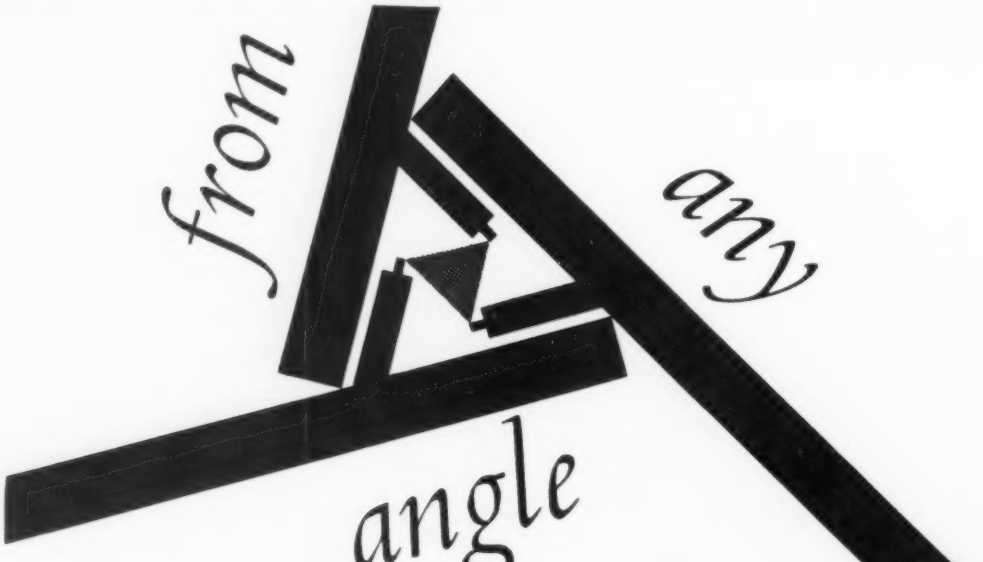

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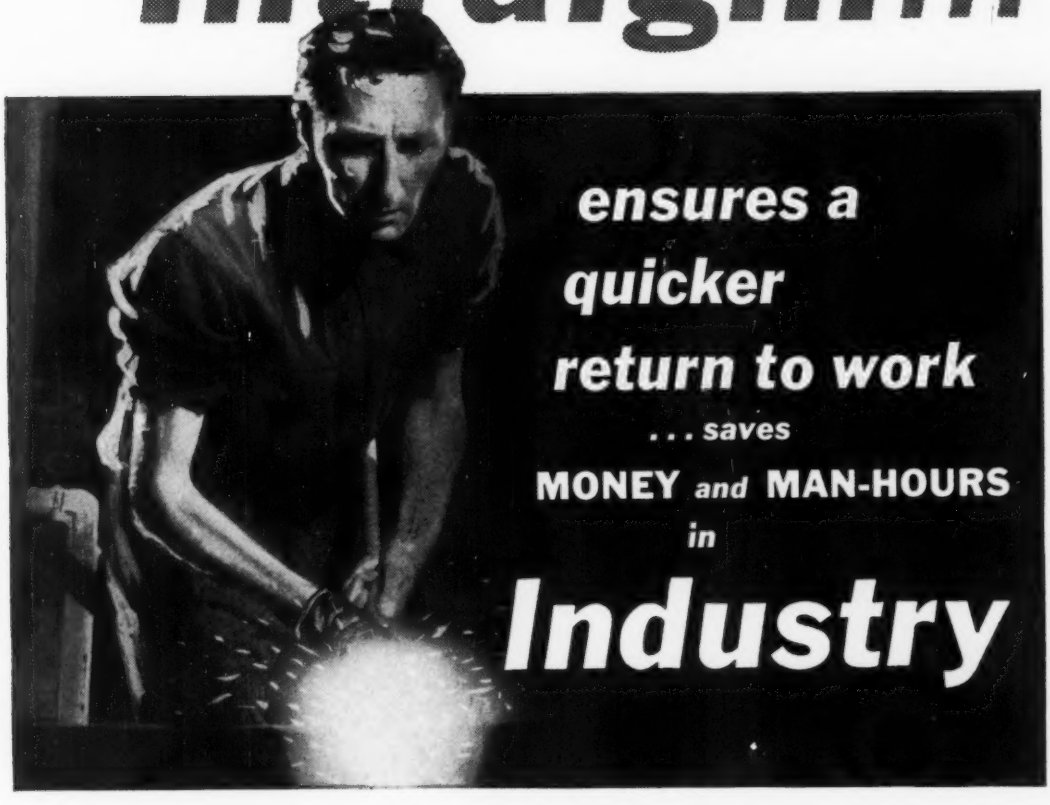

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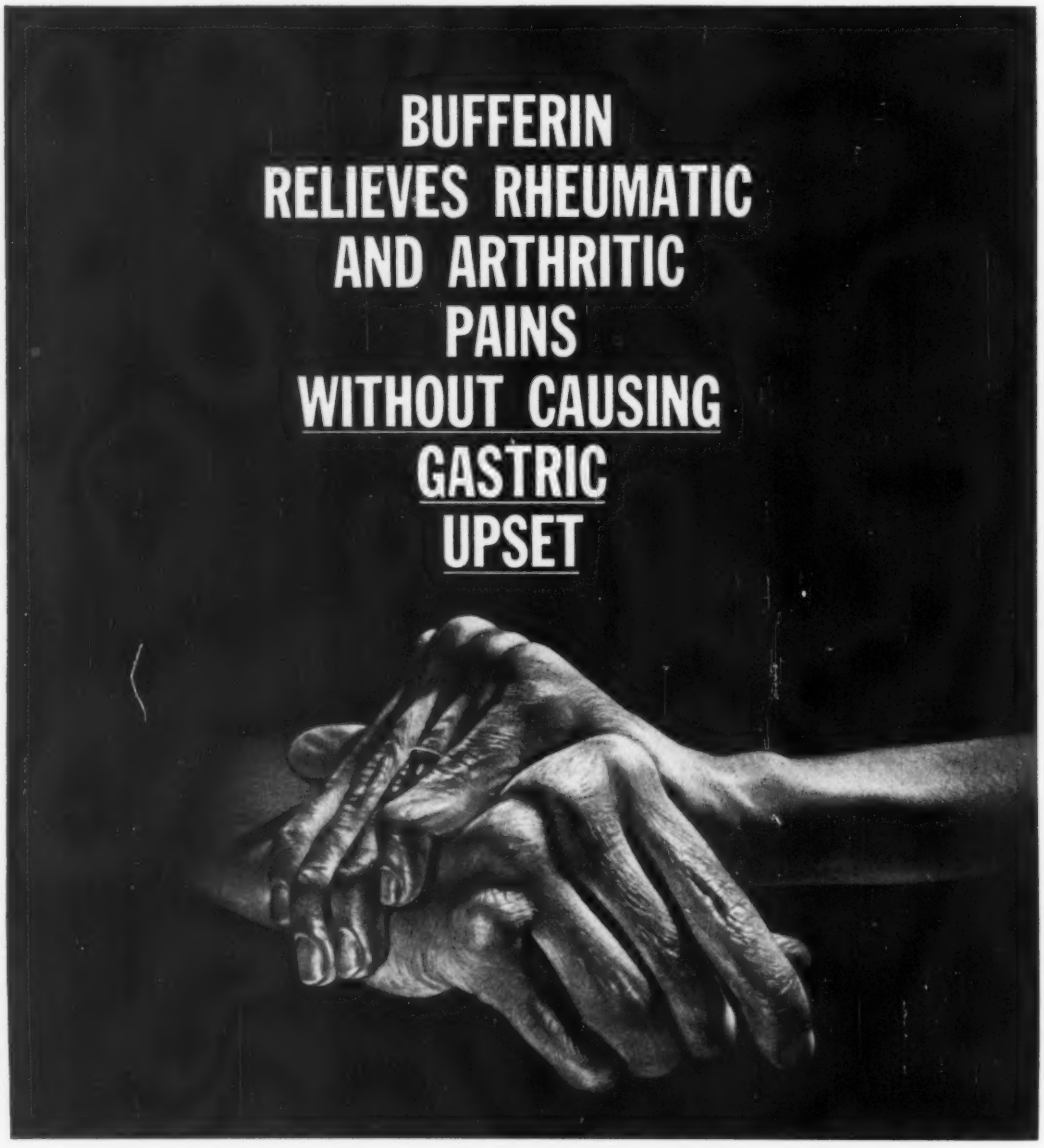

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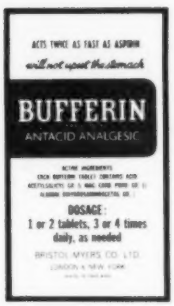

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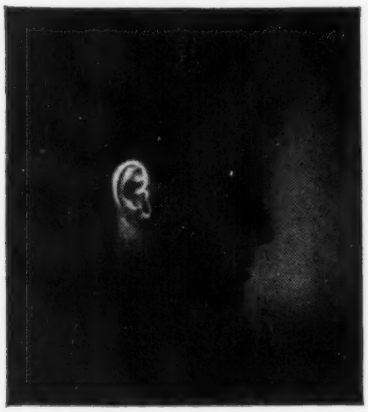

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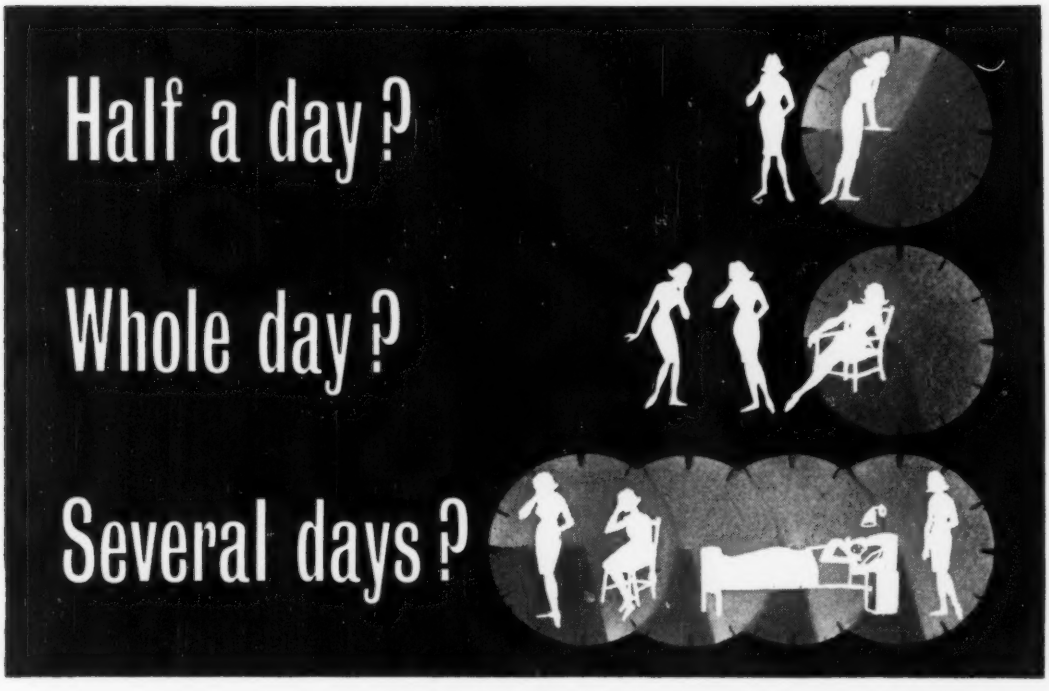

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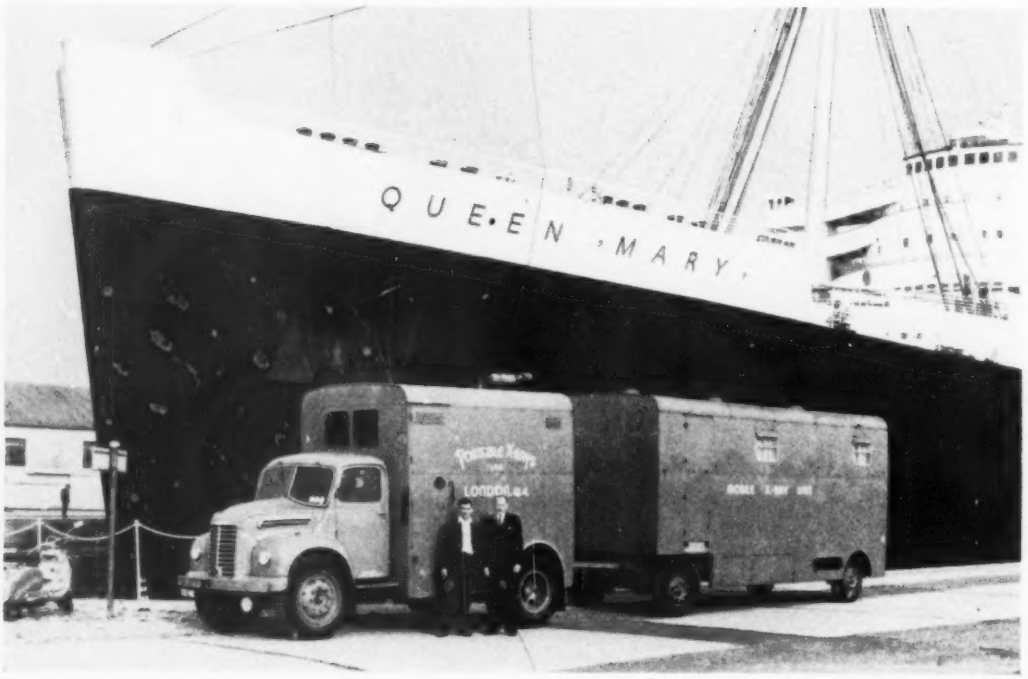

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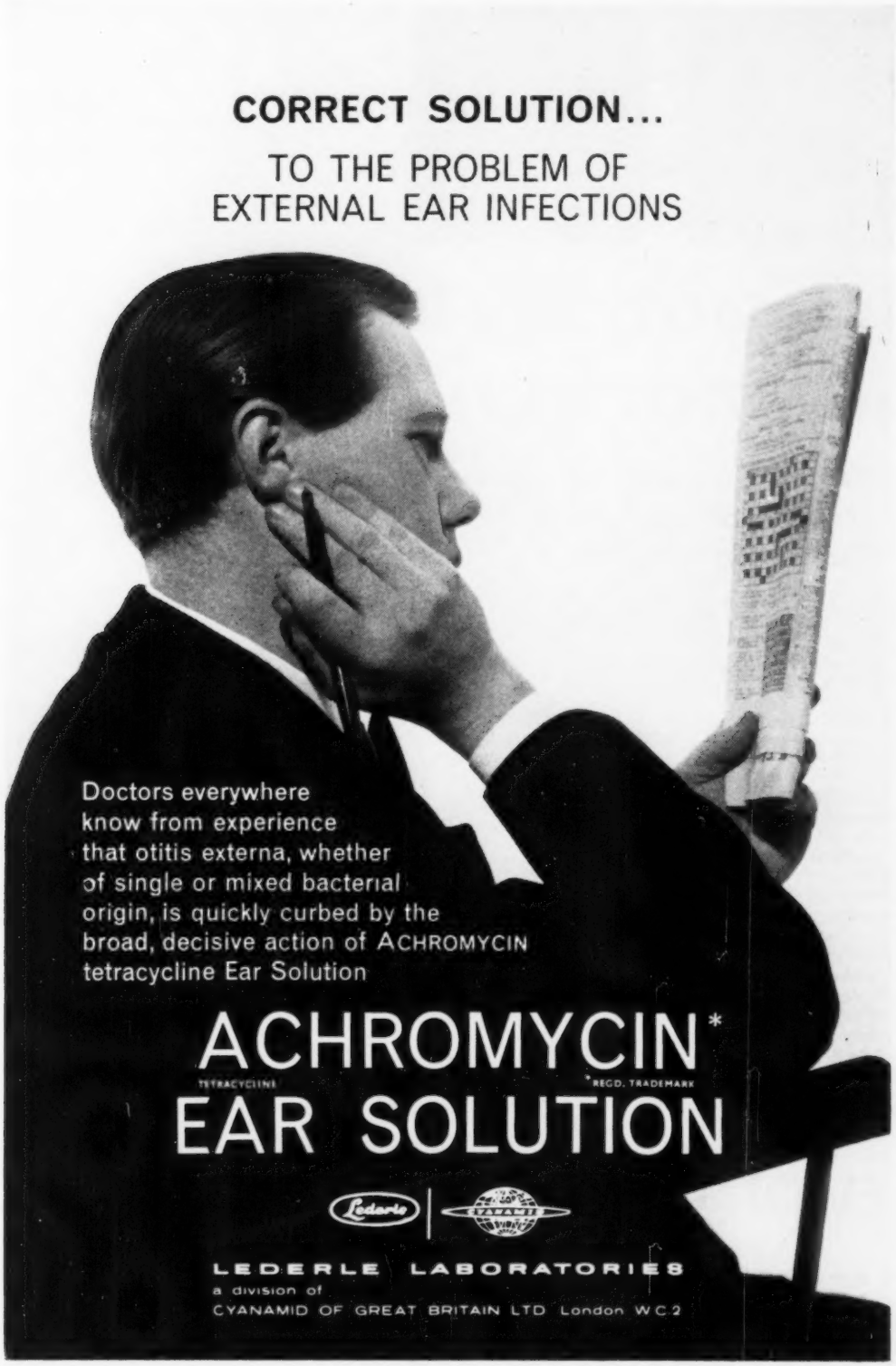

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References: "Clinical Medicine" Vol. 5, No. 4, April 1958: and "Ohio State Medical Journal," Vol. 55, No. 6, June, 1959.

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"SOOTY MANCHESTER" AND THE SOCIAL-REFORM NOVEL 1845-1855

AN EXAMINATION OF *SYBIL*, *MARY BARTON*, *NORTH AND SOUTH*, AND *HARD TIMES**

BY

ARTHUR POLLARD

From the Department of English, University of Manchester

(RECEIVED FOR PUBLICATION JANUARY 6, 1961)

"Sooty Manchester—it too is built on the infinite Abysses: overspanned by the skyey Firmaments; and there is birth in it, and death in it;—and it is every whit as wonderful, as fearful, unimaginable, as the oldest Salem or Prophetic City." (Carlyle, *Past and Present* III, xv†)

It was because others discovered this truth at about the same time as Carlyle, whose *Past and Present* came out in 1843, that there arose that succession of novels about social conditions that begins with Disraeli's *Sybil* and goes on into the next decade and even into the sixties. The creative imagination was stimulated by the social conscience, and in the product of that event "sooty Manchester"—whether it have as fictional approximation Milton, Mowbray, Coketown or be just itself—figures as a grim recurrent location.

Carlyle with his penchant for choosing extraordinary incidents and extravagant language to describe them would have been a match for even the most sensational of modern journalists, but we have to remember that his gifts enabled him to startle his generation into realizing what was going on amongst them. Amongst his examples at the beginning of *Past and Present* is this:

"At Stockport Assizes . . . a Mother and a Father are arraigned, and found guilty of poisoning three of their children, to defraud a 'burial-society' of some £3. 8s., due on the death of each child: they are arraigned, found guilty; and the official authorities, it is whispered, hint that perhaps the case is not solitary, that perhaps you had better not probe farther into that department of things. This is in the autumn of 1841; the crime itself is of the previous year or season. 'Brutal savages, degraded Irish', mutters the idle reader of Newspapers; hardly lingering on this incident. Yet it is an incident worth lingering on; the depravity, savagery and degraded Irishism being never so well admitted. In the British land, a human Mother and Father, of white skin and professing the Christian religion, had done this thing; they, with their Irishism and necessity and savagery, had been driven to it . . . A human Mother and Father had said to themselves: What shall we do to escape starvation? We are deep sunk here, in our dark cellar; and help is far . . . The Stockport Mother and Father think and hint; Our poor little starveling Tom, who cries all day for victuals, who will see only evil and not good in this world: if he were out of his misery at once; he well dead, and the rest of us perhaps kept alive? It is thought, and hinted; at last it is done." (I, i)

Beside the fact Disraeli's fiction is pallid in its impact, if little less sombre in its implications. Liza Gray, faced by her creditor Mrs. Mullins, calculates on "a death in our family soon—this poor babe can't struggle on much longer; it belongs to two burial clubs—that will be three pounds from each, and after the drink and the funeral, there will be enough to pay all our debts and put us all square" (*Sybil* III, iii). Carlyle's examples are striking, but they are not exceptional; or, if they are exceptional, they are so only in degree and not in kind. In a sentence which I omitted from the middle of the quotation he wrote: "Such instances are like the highest mountain apex emerged into view; under which lies a whole mountain region and land, not yet emerged." For the sharp evocation of sympathy and concern Carlyle's method of flashing the reader's attention on singular suffering and degradation is most suitable. The novelist seeks to bring forth that

*A Paper delivered to the Thackrah Club at its meeting in Manchester, November 18, 1960. Mr. Pollard is a lecturer in English Literature in the University of Manchester.

†Large roman figures are book numbers and small roman are chapter numbers.

sympathy and concern by inducing our longer, more concentrated gaze on the trials and pains of fairly ordinary people.

Disraeli visited Manchester in 1844 and Dickens a decade later, but Mrs. Gaskell lived there from her marriage in 1832 to her death in 1865. The population of Manchester and Salford grew from 90,000 to 400,000 in the first half of the nineteenth century. Much of this influx was of Irish origin, but, as Mrs. Gaskell indicates, many also came from rural areas of England and in time of strike there were " knob-sticks " from Burnley, " poor depressed men tramping in . . . to work at the condemned ' Starvation Prices '." (*Mary Barton*, c, xv). Nevertheless, this did not affect the near-preponderance of Irish. In a short but telling and painful survey, *Distress in Manchester* (1842), Joseph Adshead reported on the city in which Mrs. Gaskell had then lived for 10 years. Dealing with selected areas such as Ancoats and that between Brook Street and Oxford Street, Adshead found that four-ninths of the population was Irish (p. 12), that the average income of 2,000 families was 5s. 3¼d. per week (p. 18), and that 9,000 people were living in cellars, " most of them neither drained nor soughed. They are consequently damp, —are always liable to be flooded, and are almost entirely without the means of ventilation " (p. 14). He went on: " Frequently, different families occupy *opposite corners of the same room*, . . . Six or eight persons I witnessed inhabiting a damp cellar, males and females congregated together " (p. 15). Resort to the pawnshop was a widespread and inevitable practice (pp. 20–21). The general statements are surpassed in their pathos only by the citation of individual cases, of a widow with three children turned out of her house and her goods seized in satisfaction of rent arrears; of a dyer with a family of four children, whose wife had been lately confined, all of them having " been whole days without any food "; and, most terrible of all, the household where the father was dying and there were three small children (the eldest, aged 10) weaving till past 11 o'clock on Saturday night, coming home to find his father in his death-throes and being sent out in a state of semi-nudity to fetch a relative to the bedside.

It is surprising that the novelists did not exploit the industrial conditions under which children worked more fully. Only Mrs. Trollope in *Michael Armstrong, the Factory Boy* (1840) dealt with this subject. At the same time, however, we have to notice how little any of them dealt with the actual working conditions. This may have been the consequence of insufficient knowledge and experience, or else of their being principally concerned with the wider problems of social, as distinct from those of industrial, welfare. Certainly, if they lacked direct acquaintance, they might have had recourse to Blue Books and reports of committees—as indeed Disraeli did. He comes nearest to dealing with the horrors of child labour. In 1841 and 1842 Parliament received reports on factories, handloom weavers, truck, town housing, sanitary conditions, and the employment of women and children in mines. Disraeli probably used all of these, but it must suffice us to refer only to one. Here is a passage from *Sybil* (III, i):

" They come forth; the mine delivers its gang and the pit its bondsmen; the forge is silent and the engine is still. The plain is covered with the swarming multitude; . . . troops of youth, alas ! of both sexes, though neither their raiment nor their language indicates the difference; all are clad in male attire; and oaths, that men might shudder at, issue from lips born to breathe words of sweetness . . . But can we wonder at the hideous coarseness of their language when we remember the savage rudeness of their lives ? Naked to the waist, an iron chain fastened to a belt of leather runs between their legs clad in canvas trousers, while on hands and feet an English girl, for twelve, sometimes for sixteen, hours a day, hauls and hurries tubs of coal up subterranean roads, dark, precipitous, and plashy . . . See, too, these emerge from the bowels of the earth ! Infants of four and five years of age, many of them girls, pretty and still soft and timid; entrusted with the fulfilment of responsible duties, and the nature of which entails on them the necessity of being the earliest to enter the mine and the latest to leave it. Their labour indeed is not severe, for that would be impossible, but it is passed in darkness and in solitude . . . Hour after hour elapses, and all that reminds the infant trappers of the world that they have quitted and that which they have joined is the passage of the coal wagons for which they open the air doors of the galleries, and on keeping which doors constantly closed, except at this moment of passage, the safety of the mine and the lives of the persons employed in it entirely depend."

It is sufficient to place alongside this passage one or two quotations from the *First Report* (*Mines*) *of the Children's Employment Commission* (1842):

" 121. . . . ' One of the most disgusting sights I have seen was that of young females, dressed like boys in trousers, crawling on all fours, with belts round their waists and chains passing between their legs '. (Statement by Sub-Commissioner in the West Riding of Yorkshire.)

Conclusions

. . . In regard to Coal Mines—

1. That instances occur in which children are taken

into these mines to work as early as four years of age . . .
7. That the nature of the employment which is assigned to the youngest children, generally that of " trapping ", requires that they should be in the pit as soon as the work of the day commences, and, according to the present system, that they should not leave the pit before the work of the day is at an end.
8. That, although this employment scarcely deserves the name of labour, yet, as the children engaged in it are commonly excluded from light and are always without companions, it would, were it not for the passing and re-passing of the coal carriages amount to solitary confinement of the worst order.
11. That, in the districts in which females are taken down in to the coal mines, both sexes are employed together in precisely the same kind of labour and work for the same number of hours; that the girls and boys, and the young men and women, and even married women with child, commonly work almost naked, and the men, in many mines, quite naked; and that all classes of witnesses bear testimony to the demoralising influence of the employment of females underground."

But even here Disraeli is content to comment; he does not attempt to dramatize, as he does for instance, in his treatment of the evils of the truck system. And great as was the potential of this report, what might have been made of the 1832 report on factory children with its revelation of children working regularly from 6 a.m. to 8.30 p.m. and at busy periods from 3 a.m. to 10 p.m. with only a total of one hour off for meals and all this for 3s. and 3s. 7½d. per week, with its account of severe penalties for being late by as little as five minutes and of serious accidents as a result of fatigue, of crippling deformities, and premature death ? The conscience of Victorian England woke up to two generations of merciless exploitation, and not before it was time.

When he wishes, Disraeli can not only describe, but also convey the spirit of, a scene very well. His treatment tends to be episodic and, as a result *Sybil* covers a wider area of activity than the other social novels. At one time it is the village life of Marney, rural but by no means idyllic (I, iii), at others the scramble and tyranny of the truck shop (III, iii), the model factory of Mr. Trafford (III, viii) or the barren Wodgate with its semi-heathen community (III, iv). The ability to describe so wide a range is the product of Disraeli's observation and intelligent reporting; the corresponding drawback, however, is a certain loss of concentration and of intimate understanding of personal predicaments. The characters are looked at from outside and even from there not for long enough. They are often little more than passing acquaintances. Occasionally, however, Disraeli attains a noticeable power within an episode. Nowhere is this better illustrated than in the description of a handloom weaver Warner and his family (II, xiii).

" It was a single chamber . . . In the centre placed so as to gain the best light which the gloomy situation could afford, was a loom. In two corners of the room were mattresses placed on the floor . . . In one was his sick wife; in the other, three young children: two girls, the eldest about eight years of age; between them their baby brother. An iron kettle was by the hearth, and on the mantelpiece, some candles, a few lucifer matches, two tin mugs, a paper of salt and an iron spoon. In a farther part, close to the wall was a heavy table or dresser; this was a fixture, as well as the form which was fastened by it.

The man . . . looked around him at his chamber without resources: no food, no fuel, no furniture, and four human beings dependent on him, and lying in their wretched beds, because they had no clothes."

Warner reflects on past sufficiency and present sufferings, on his broken-spirited wife and starving children, on the conflict between the instinct for survival and the temptation to crime, on a prospect even bleaker than the pitiable present. All this is powerfully suggested; the oscillations of Warner's inner struggle, the hopelessness of his wife, the pathetic state of the children with the baby comforted with the last morsel of a crust soaked in water and tied in a cloth for him to suck. Detail such as this last has a very authentic ring. Moreover, this scene and these characters are in the central line of the novel's development, unlike the descriptions of the mines and the truck-shop, which, though quite effective, represent a kind of superadded demonstration of social evil.

Mrs. Gaskell, though she is undisciplined in other directions, does not dissipate her creative energy in this one. *Mary Barton* was written out of avowed " sympathy with the careworn men, who looked as if doomed to struggle through their lives in strange alternations between work and want" (Preface). Possessed of a knowledge, or more correctly of a sort of knowledge, to which neither Dickens nor Disraeli could lay claim, she delineated accurately the Manchester she knew so well; Berry Street, for example, " unpaved: and down the middle a gutter forced its way, every now and then forming pools in the holes with which the street abounded . . . As they passed, women from their doors tossed household slops of *every* description into the gutter . . . Heaps of ashes were the stepping-stones, on which the passer-by, who cared in the least for cleanliness, took care not to put his foot ", and on to Davenport's cellar " very dark inside.

The window-panes many of them were broken and stuffed with rags ", the foetid smell, " the thick darkness of the place " and " the three or four little children rolling on the damp, nay wet brick floor, through which the stagnant, filthy moisture of the street oozed up " (*Mary Barton*, c. vi). The parallel of this description of the cellar with that given by Adshead and quoted earlier, the parallel, that is, of fiction and fact is obvious. The extra detail of the fiction serves only to make it more vivid. Confirmation of Mrs. Gaskell's faithfulness to actuality in her description of the street is provided by another witness, the surgeon John Robertson, in his evidence about Manchester to the Committee on the Health of Towns (1840) with his references to streets badly drained, " full of pits, brimful of stagnant water, the receptacle of dead cats and dogs ". In his testimony Robertson quoted a pamphlet by a fellow doctor, J. P. Kay (later Sir James Kay-Shuttleworth) now remembered for his work as secretary to the Privy Council's committee on education. I mention his name however, because he was a friend of Mrs. Gaskell's. Robertson's evidence also contains reference to Manchester's having no public park and to the rapid expansion of the city so that " those who live in the more populous quarters can seldom hope to see the green face of nature ". Facts such as these give added importance to the manner in which Mrs. Gaskell chose to open her " tale of Manchester life " with its description of Green Heys Fields, " these commonplace but thoroughly rural fields " with here and there a black-and-white farmhouse, with " the lowing of cattle, the milk-maid's call, the clatter and cackle of poultry," the flowers and hedges, the place of picnic. We remember this during our sustained and sombre acquaintance with Berry Street and its like in the body of the novel. Mrs. Gaskell was adept in the implications of contrast. In *North and South* the poverty of people like the Higgins and the Bouchers comes out the more strikingly as we contemplate the vulgar ostentation of the Thorntons' drawing-room.

Mrs. Gaskell's scenes are built up stage by stage by an accumulation of detail. It is therefore possible quite easily to notice the contrasts. Dickens does not seek his effects in this manner. His method is altogether less patient; his detail is of the sharp and isolated kind. Not for him the laboriously faithful catalogue technique, but rather the single fact. As the weaver Stephen Blackpool calls on his employer, Mr. Boundery " at lunch on chop and sherry "—not even a verb to complete the sentence (*Hard Times* I, xi). Dickens perhaps skilfully avoided detailed description. He did not know his Lancashire well enough. He went to Preston in 1852 to see a strike in progress, but he soon returned home after finding " very little in the streets to make the town remarkable " (Forster, *Life of Dickens* III, 49). Certainly when he gives us details, we often want to question them. Allowing that Stephen Blackpool was as intelligent as Dickens sometimes suggests (and at other times he appears remarkably uninformed), one wonders about those " few books and writings . . . on an old bureau in the corner " (I, x). There were learned workmen—Mrs. Gaskell's Job Legh was one of them—, but Dickens' detail is here not to describe the place where Stephen lived or even to tell us something about him, but to contrast with his drunken wife, the sorrow of his life, who has suddenly reappeared and is there before him lolling almost insensibly on a chair. Here, of course, is a contrast, but it is achieved by a method, in a direction and with a purpose and effect quite different from those of Mrs. Gaskell. Dickens' skill at his craft made him seek that which made the town remarkable. This search after the remarkable is seen in the initial description of Coketown. The view is panoramic, the method is that of broad strokes and strong colours:

" Coketown, to which Messrs. Bounderby and Gradgrind now walked, was a triumph of fact; it had no greater taint of fancy in it than Mrs. Gradgrind herself. Let us strike the key-note, Coketown, before pursuing our tune. It was a town of red brick, or of brick that would have been red if the smoke and ashes had allowed it; but as matters stood it was a town of unnatural red and black like the painted face of a savage. It was a town of machinery and tall chimneys, out of which interminable serpents of smoke trailed themselves for ever and ever, and never got uncoiled. It had a black canal in it, and a river that ran purple with ill-smelling dye, and vast piles of buildings full of windows where there was a rattling and trembling all day long, and where the piston of the steam-engine worked monotonously up and down like the head of an elephant in a state of melancholy madness. It contained several large streets all very like one another, and many small streets still more like one another, inhabited by people equally like one another, who all went in and out at the same hours, with the same sound upon the same pavements, to do the same work, and to whom every day was the same as yesterday and to-morrow, and every year the counterpart of the last and the next. " (I, v)

None can miss the power by which the frightening monotony of the whole place is suggested. There is one phrase, however, which immediately measures Dickens' distance from his subject; it is: " inhabited by people equally like one another ". The likeness of Manchester to everywhere else, Carlyle reminded

us, is in the universal and fundamental—" there is birth in it, and death in it "; but that phrase reminds us also that the universal and fundamental is but an agglomeration of innumerable individuals. Dickens did not see this; he did not see the individual as he was. Indeed, the common Dickensian method of characterization by caricature is, in one aspect, a failure to see the individual in his fullness.

Method reflects purpose, and it is well therefore with this comment on Dickens that we should clearly distinguish what our three novelists were trying to achieve. Dr. Leavis in his penetrating, though somewhat too laudatory, estimate of *Hard Times* has described the novel as a moral fable (*The Great Tradition* 1948, p. 227), and the last paragraph certainly indicates the didactic intention. The value of Leavis's comment is to direct our minds to the way in which places, events, and people in the novel are to be regarded. The fable teller concentrates upon essentials and arranges them with their single insistent meanings into a significant pattern. *Hard Times* is an attack on Fact, on Benthamite utilitarianism and its practical application in the debased commercial materialism of the mid-nineteenth century. Of all this Coketown is the hideous architectural symbol, Bounderby its hard-faced apostle and the workers of Coketown its mass of mute and nameless victims. Dickens was attacking the whole system, and so was Disraeli; but with him there was little of Dickens' concentration but much of an ulterior purpose. He too attacked the system whose glorification of freedom brought such semi-slavery and degradation, but for him there was a political alternative which would heal the breach which unnaturally divided " the two nations " of Englishmen. His work draws upon political information and looks towards a partly political solution. Moreover, the peculiar position of Sybil herself brings in an extra dimension. Mysterious, romantic, religious, she is deliberately and often unexpectedly dramatized. Through her the hope of a partly religious solution is projected into the book. Dickens' picture is a dark one; in Disraeli's there are always rays of light. At the end of the passage describing Warner's sufferings there comes a knocking at the door " and there entered SYBIL " (II, xiii). The thesis obtrudes more prominently in this novel than in the others, much more for instance, than in *North and South* or *Mary Barton* where Mrs. Gaskell is anxious to stress the need for greater mutual understanding between employers and employed. The measure of success she achieves derives from the same quality within her which dictated the nature of the solution she propounded, namely, her deep sympathy springing from an interaction of her humanity with her intimate knowledge of the things about which she wrote. That is why with her we are more aware of actual relationships of actual people.

We must therefore now consider characterization. In general, these novelists recognized that three-fold division of society, Barbarians, Philistines, and Populace, which Matthew Arnold noted in *Culture and Anarchy*. For him the Barbarians or aristocracy were bent upon field-sports and honours, the Populace on beer and brawling, and the Philistines or middle-class on money-making and Methodist tea-meetings. Neither Mrs. Gaskell nor Dickens is much occupied with the aristocracy—in *North and South* the frivolous occupations of her London relatives set off for Margaret the seriousness of life in Milton and in *Hard Times* the bored fatalism and total lack of principles of James Harthouse are utilized in the plot,—but for Disraeli the place of aristocracy is central, not the effete and corrupting aristocracy of the Marneys and the Mowbrays but the rightful idealist aristocracy of Sybil. The triumph of this latter is symbolized at the end in the destruction of Mowbray Castle by fire, the union of the religious Sybil and the political idealist Egremont and the recovery of the documents proving the right of Sybil's family to the Mowbray lands. Again, unlike the other two, Disraeli has a definite place for the Church. The ruins of Marney Abbey are a symbol of the work which the Church once had in the daily life of the community and of the fact that it no longer fulfilled this work; and the presence of the Tractarian St. Lys is a continual self-critical commentary on the Church's shortcomings in failing to perform its social obligations.

The chief interest of all three novelists lies, however, in the middle and lower classes, the manufacturers and workmen, and the constant struggle between them.

" The Working Aristocracy; Mill-owners, Manufacturers, Commanders of Working Men: alas against them also much shall be brought in accusation; much—and the freest Trade in Corn, total abolition of Tariffs, and uttermost ' Increase of Manufactures ' and ' Prosperity of Commerce ' will mend no jot of it. The Working Aristocracy must strike into a new path; must understand that money alone is *not* the representative either of man's success in the world, or of man's duties to man; and reform their own selves from top to bottom." (*Past and Present* III, viii)

Thus Carlyle, and thus the burden also of our novelists. Here again Disraeli differs from Dickens and Mrs. Gaskell. They have little about the aristocrats; he has little about the manufacturer as such. Dickens, on the other hand, has the bad master in Bounderby, pompous, egotistical, stupid

and cruel. For Bounderby the workers were " Hands ", so many units in a mass,

" something to be worked so much and paid so much, and there ended; something to be infallibly settled by laws of supply and demand; something that blundered against those laws, and floundered into difficulty; something that was a little pinched when wheat was dear and over-ate itself when wheat was cheap; something that increased at such a rate of percentage, and yielding such another percentage of crime, and such another percentage of pauperism; something wholesale, of which vast fortunes were made; something that occasionally rose like a sea and did some harm and waste (chiefly to itself) and fell again." (*Hard Times* II, vi)

So Louisa Bounderby (née Gradgrind) had been taught to regard them in the course of her " fact " - circumscribed education. So her husband regarded them, with an admixture of contempt and even hatred. Louisa, in the course of the book, is emancipated from these arid, emotionless generalities, and led to show that kindness which she possesses and which her husband so monstrously lacks. Mrs. Gaskell's employers are hard, but they are never inhuman. Carson in *Mary Barton*, though he swears terrible vengeance on his son's murderer, is reconciled with John Barton on the latter's death-bed, and in *North and South* (probably being careful to forestall a recurrence of some of the criticisms levelled against her first novel) Mrs. Gaskell is at pains to stress the humanity of Thornton. This does not mean that she fails to portray what she regards as the limitations of his class. Indeed, these limitations help to make him convincing. He genuinely believes in the inescapable operations of the trade-cycle (c, xix), in the opportunities for economic self-advancement and in the battle of masters and men (c, x). Mrs. Gaskell writes understandingly of him—" Of course, speaking so of the fate that, as a master, might be his own in the fluctuations of commerce, he was not likely to have more sympathy with that of the workmen " (c, xix); and she is anxious to speak justly of him. When in the pique of argument he quibbles momentarily, she has him recover immediately: " His straightforward honesty made him feel that his words were but a poor and quibbling answer to what [Margaret] had said, and, be she as scornful as she liked, it was a duty he owed to himself to explain, as truly as he could, what he did mean " (c, x). Thornton eventually learns partly from Margaret and, through her, partly from the workman Nicholas Higgins something of the lot of the workers, and he takes practical steps to help them by instituting a system of bulk-buying and communal cooking.

These novelists are concerned to stress that much of the trouble arises from a failure in communication, in the ignorance and the inability to imagine on the part of one half the way in which the other half of the world lives. Inhuman theories and social isolation stifle sympathy. The trouble, however, is seen to be by no means all on the masters' side. The workers, too, are the victims of inadequate understanding and sometimes even of deliberate misinterpretation. The Trade Unions and Chartism, in particular, come under severe attack. Disraeli has much to say about the Chartist agitation of 1839 and of the willingness of its leaders to exploit suffering for their own ends. The destructive outburst of the Wodgate Hell-cats is the direct result of Chartist instigation (VI, vii). Chiefly, however, attention is concentrated on the exploitation of power by the Trade Union leaders. This is seen in the hollow insincerities and the glib rhetoric of the agitator Slackbridge in *Hard Times*. With an inflated style and ample recourse to exclamation and rhetorical question, with skilful alternation of appeals to flattery, fear, loyalty, and the instinct to attack, Slackbridge brings the workers to cast off Stephen Blackpool, to send him to Coventry. Slackbridge is described as a somewhat repulsive figure; he is openly criticized as a character lacking the integrity and nobility of those he misleads ; his address to " friends and brothers " is shot through with ironic condemnation, and his fluent dishonesty is only the more evident by contrast with the halting ineffectual defence of the man he is persecuting. (See, *e.g.* II, iv; III, iv.) Mrs. Gaskell also dwells on the isolation of a man from his fellows on the orders of the Union:

" If a man doesn't belong to the Union, them as works next looms has orders not to speak to him—if he's sorry or ill it's a' the same; he's out o' bounds, he's none o' us; he comes among us, he works among us, but he's none o' us. I' some places them's fined who speaks to him. Yo' try that, miss; try living a year or two among them as looks away if yo' look at 'em." (*North and South*, c, xxviii)

Mrs. Gaskell again gains the effect so justly and so succinctly. She also emphasizes the conspiratorial aspect of the Unions, for example, in the dark plottings, " strange faces of pale men, with dark glaring eyes ", the beckoning of a hand within the door in *Mary Barton*. " They were all desperate members of Trades' Unions, ready for anything "; but, she goes on, " made ready by want " (c, x). Beside this Disraeli's account of a Union committee at work appears theatrical, meeting at a secret rendezvous, disguised in dark cloaks and black masks, denouncing offending

workmen and masters alike, planning vengeance against them, conducting demonic initiation rites and binding their members even to murder (*Sybil* IV, iv). That this last did happen—or that the novelists believed it to happen—is shown also by the lot John Barton drew which required him to kill young Carson. Here again, however, with the emphasis upon the strain which the demand represents in the life of an individual with whose history and feelings we are intimate, Mrs. Gaskell's treatment of the matter appears more convincing than that of Disraeli. The common element underlying the criticism of the Trade Unions is the objection to the oppression of the individual which their activity brings about. Stephen Blackpool in *Hard Times* is excluded and thereby driven from the company of his fellows; the pitiable Boucher in *North and South* is compelled to join, to participate unwillingly in a strike and finally, in desperation at his family's sufferings, to drown himself; John Barton is led to commit murder and die of remorse.

Histories such as these remind us that in the kind of novel with which we are here concerned there is a strong tendency to predispose both character and action to fit the thesis. Dickens especially was prone to this, and in *Hard Times* there is a simple, perhaps over-simplified, distinction of the rich and villainous on the one hand and the poor and virtuous on the other—Slackbridge alone excepted. Mrs. Gaskell, after the criticism of *Mary Barton*, sought a less biased position in *North and South*, whilst Disraeli (this is one virtue of his wide range of reference) included characters of varying degrees of worth at the different social levels he considered. Mrs. Gaskell and Disraeli, however, used characters for the benefit of their commentary in other ways. Esther, the prostitute, aunt to Mary Barton, is little more than a lurid object-lesson of the end to which flighty young girls who listen to smooth-tongued would-be seducers inevitably arrive; whilst in Sybil herself there is a strong fairy-godmother element. Mention of Sybil also reminds us that there is a method by which Mrs. Gaskell and Disraeli seek a reliable, superior and detached commentator position within the novel itself by the use of a suitable character. Sybil herself in some ways fulfils this role, but the better example is that of Margaret Hale in *North and South*, the outsider knowing places other than Milton, acquainted with both sides of industry through her friendships with master and men but not involved with or sharing the prejudices of either side. Yet another technique of characterization to be noted is the use made of children and young people, especially in their suffering. Dickens rather surprisingly, considering what he does elsewhere, makes little of this in *Hard Times*, but what Disraeli does we have seen already and Boucher's family in *North and South* has also been mentioned. More prominent, however, is the suffering of Bessy Higgins in this novel. There is a noble fortitude and a moving strain of piety in her character.

The use of characters such as these had both its strength and weakness. The latter is manifested in sentimentality, moralizing and melodrama. It is easy to overpaint the suffering for ulterior effect; it is easy to idealize a character to point a lesson; it is easy, too, to refuse to follow out the logic of suffering in the mistaken desire to spare the reader's feelings. Mrs. Gaskell—perhaps this is a mark of her humanity, or perhaps only of her femininity—is prone to these faults, though we must not forget Dickens' climax with the death of Stephen, referring in his dying words to Rachel's long-dead little sister and to shining stars that point beyond the present muddle. Even symbolic interpretation does not clear away the incongruities of inescapable actuality here; and the bringing-in of references to the star of Bethlehem and the chapter's last sentence—"The star had shown him where to find the God of the poor: and through humility, and sorrow, and forgiveness, he had gone to his Redeemer's rest"—may give the right aura of divine comfort at the last, but they do not issue necessarily out of what has gone before.

This sort of failure, like the exploitation of helpless suffering in children, points us also to strength, indeed the radical source of strength, the very inspiration out of which these novels issued, namely, an intense sympathy with suffering mankind and a strong desire for the amelioration of the human condition. The evil thing that separates, the baffling isolation of man from his fellow men, is what all these novels attack. As one might expect, it is Disraeli the politician who most precisely envisages a social and political solution, but he with the others sees that basically the problem is a moral one. Rachel puts it to Louisa in *Hard Times*: "The like of you don't know us, don't care for us, don't belong to us" (III, iv), but Rachel is only partly right. There may be ignorance or mis-understanding, but there is no necessary indifference or inevitable separation. Disraeli speaks of "the community of purpose that constitutes society" (*Sybil* II, v). Men had to recognize that truth, and in doing so they had also to recognize the concomitant truth that each man is an inviolable entity; in Stephen Blackpool's words, not "Rating 'em as so much Power, and reg'lating 'em as if they was figures in a soom, or machines: wi'out loves and likens, wi'out memories and inclinations,

wi'out souls to weary and souls to hope", but "drawin' nigh to fok, wi' kindness and patience an' cheery ways" (*Hard Times* II, v). A system that produced the evil which these writers lament had to be changed. Labour had its rights as well as its duties (as Disraeli reminded the electors of Shrewsbury in 1843); and these rights, the basic human dignities, could not continue to be flouted, they would have again to be regarded. I began with Carlyle; let me end with him, for his is a seminal mind in this phase of English history.

"Men cannot live isolated: we *are* all bound together, for mutual good or else for mutual misery . . . In this world there is one godlike thing, the essence of all that was or ever will be godlike in this world: the veneration done to Human Worth by the hearts of men." (*Past and Present* IV, vi)

With this attribute Dickens, Mrs. Gaskell and Disraeli were abundantly endowed.

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CHRONIC RESPIRATORY DISEASE IN A RANDOM SAMPLE OF MEN AND WOMEN IN THE RHONDDA FACH IN 1958

BY

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To investigate the high death rates for bronchitis in South Wales miners a survey of respiratory symptoms and ventilatory capacity in 90% of a random sample of 600 men between the ages of 35 and 64 and 200 women between 55 and 64 living in the Rhondda Fach was carried out. The sample of men was stratified by age and occupation, 100 miners and ex-miners, and 100 non-miners being studied in each decade.

The higher prevalence of symptoms and lower mean indirect maximum breathing capacity (I.M.B.C.) of the miners and ex-miners, observed previously, was confirmed and within the mining group there was little relation of symptoms to radiological category of pneumoconiosis. Miners and ex-miners with progressive massive fibrosis had a lower mean I.M.B.C. than the rest at all ages.

Analysis of symptoms and I.M.B.C. by length of time spent working on the coal-getting shift in both miners and ex-miners did not suggest that the total dust dosage to which a man had been exposed during his working life was closely related to chronic respiratory disease. A lower prevalence of symptoms and a higher mean indirect M.B.C. was found in those who had worked for under one year on the coal-getting shift. Above one year no clear pattern of symptom prevalence was discerned although there was a slight downward trend in the mean indirect M.B.C. with increased time spent working on the coal-getting shift. When working miners alone were considered the reduction in ventilatory function with increasing duration of work was slightly greater.

Dust exposure alone seemed unlikely to account for all the excess respiratory disease in miners compared with the rest of the community and other possible explanations are discussed.

The women recorded a lower prevalence of symptoms than the men who had never worked in mining. This prevalence was, however, higher than that previously found in rural areas in Wales and Scotland. The mean indirect M.B.C. recorded for the women in this survey was also lower than that observed in Scots women.

Analysis of the findings in the women according to the occupation of their husbands showed that miners' wives recorded a higher prevalence of symptoms and lower mean indirect M.B.C. than non-miners' wives, suggesting the importance of social rather than occupational factors in miners.

Smoking was associated with an increased prevalence of symptoms and lower indirect M.B.C. in the men but not in the women. Differences in smoking habits could not, however, account for the differences between miners and non-miners, as these remained after standardization for smoking.

National mortality rates suggest that South Wales coal-miners are unduly prone to bronchitis. The standardized mortality ratios (S.M.R.) for bronchitis of miners between the ages of 20 and 64 were 254 in the anthracite area and 207 in the rest of Glamorgan (Registrar-General, 1958), figures which may be compared with 147 for Cheshire and Lancashire, and 80 for Derbyshire (Higgins, Cochrane, Gilson, and Wood, 1959). While these mortality statistics are of course liable to some regional variation in death certification, they rank the areas for chronic respiratory disease in the same order as our morbidity studies (Carpenter, Cochrane, Gilson, and Higgins, 1956; Higgins, Oldham, Cochrane, and

Gilson, 1956; Higgins, *et al.*, 1959) of random samples of the community have done and it seems justifiable therefore to accept them as a reasonably close approximation to the truth. The question that immediately follows is: Why should South Wales coal-miners have between two and three times as much bronchitis as coal-miners in other areas ?

In 1954 we attempted a study of bronchitis in a random sample of men in the Rhondda Fach using a standardized questionnaire. The sample investigated at that time was small and subsequent modification of the questionnaire has made it difficult to compare the results in the Rhondda with those established in later surveys in other areas of Great Britain. The obvious desirability of providing comparable results for the Rhondda and the expectation that aetiological factors should be more obvious in an area where the disease prevalence is highest led us to undertake a further study of respiratory disease there in 1958. This paper records our findings.

The Random Sample

The population of the Rhondda Fach, originally enumerated by private census by Cochrane and his colleagues (Cochrane, Cox, and Jarman, 1952), was rechecked in 1958. The sample studied was drawn using random numbers from this population.

It consisted of 600 men between the ages of 35 and 64. In each decade there were 200 men, 100 miners and ex-miners, and 100 men who had never worked in mining. Previous radiological studies (Cochrane *et al.*, 1952; Cochrane, Davies, Chapman, and Rae, 1956) suggested that of the 100 miners and ex-miners there would be about 50 with and 50 without pneumoconiosis and that of those with pneumoconiosis about 10 would have progressive massive fibrosis.

In order to investigate further the high S.M.R. from bronchitis of miners' wives, to which the Registrar-General has alluded in his last two Decennial Mortality Supplements (Registrar-General, 1938 and 1958) we included a random sample of 200 women between the ages of 55 and 64. The number of men and women living in the area, the number sampled, the response rate, and number finally analysed are shown in Table 1.

Methods and Procedure.—The methods and procedure were similar to those used previously (Higgins and Cochran, 1958). Respiratory symptoms were recorded using a questionnaire comparable with that used on all previous surveys except the Rhondda investigation of 1954 already mentioned (Higgins *et al.*, 1956; 1959). The questionnaire was essentially the same as that recently approved by the Medical Research Council's Bronchitis Committee. Occupational histories from the time of leaving school and domiciliary histories from birth were obtained. The 0·75 second forced expiratory volume ($F.E.V._{0.75}$) was measured and expressed as the indirect maximum breathing capacity (I.M.B.C.) by multiplying by 40 (McKerrow, McDermott, and Gilson, 1960). Standing and sitting heights and weights were measured and a postero-anterior chest radiograph was taken.

Members of the sample were visited in their homes and asked to participate in the investigation. Appointments were made and transport to and from the hall where the tests were carried out was offered.

Results

Table 2 shows the mean ages and main measurements in each group. The decline in mean height with age noted previously in the Vale of Glamorgan (Higgins, 1957) is again seen. The miners and ex-miners over 45 years were on the average significantly shorter and at all ages lighter than the corresponding non-miners. The mean heights of the non-miners are half to one inch above those found in the survey of the population of Great Britain carried out by the Ministry of Food (Kemsley, 1950) in 1943.

TABLE 1
RANDOM SAMPLE STRATIFIED BY AGE AND OCCUPATION

Occupation	Age Group	No. in Population at Census*	No. Sampled	Dead	Left Area	Refused	Not Seen	Seen	Excluded†	Added from Other Groups	Finally Analysed
Non-miners	35–44	495	100	0	6	9	0	85	1	4	88
	45–54	338	100	1	2	8	1	88	3	3	88
	55–64	146	100	0	0	9	2	89	4	1	86
Miners and ex-miners	35–44	1,127	100	0	2	8	0	90	4	0	86
	45–54	1,283	100	0	0	5	0	95	3	3	95
	55–64	1,114	100	3	0	4	1	92	1	3	94
Women	55–64	1,535	200	4	1	12	8	175	2	0	173

* Date of Census June 1, 1958.
† Because age or occupational history was found to be incorrect.

TABLE 2

MEAN AGE AND MEASUREMENTS

Occupation	Age Group	No.	Age (years)	Standing Height		Sitting Height		Weight	
				in.	cm.	in.	cm.	lb.	kg.
Non-miners	35–44	88	39·5	67·1	170·4	35·3	89·7	154·7	70·2
	45–54	88	49·7	66·7	169·4	35·1	89·2	154·6	70·1
	55–64	86	59·4	66·4	168·7	34·4	87·4	148·0	67·1
Miners and ex-miners	35–44	86	40·1	67·0	170·2	35·4	89·9	147·7	67·0
	45–54	95	49·5	65·9	167·4	34·7	88·1	144·2	65·4
	55–64	94	59·9	65·5	166·4	34·1	86·6	140·1	63·5
Women	55–64	173	59·7	60·9	154·7	32·2	81·8	145·3	65·9

TABLE 3

PREVALENCE OF PNEUMOCONIOSIS IN THE RHONDDA FACH MINERS AND EX-MINERS IN SAMPLE 1958

Age Group	Radiological Category						Total
	0	1	2	3	All Simple Pneumoconiosis	P.M.F.	
35–44	36 (41·9)	18 (20·9)	13 (15·1)	11 (12·8)	42 (48·8)	8 (9·3)	86 (100·0)
45–54	27 (28·4)	18 (18·9)	12 (12·6)	11 (11·6)	41 (43·2)	27 (28·4)	95 (100·0)
55–64	25 (26·6)	24 (25·5)	15 (16·0)	1 (1·1)	40 (42·6)	29 (30·9)	94 (100·1)

Percentages are given in brackets.

TABLE 4

MEAN VENTILATORY CAPACITY MEASUREMENTS IN NON-MINERS, MINERS, AND EX-MINERS ACCORDING TO AGE

Occupation	Age Group	I.M.B.C. (litres/min.)	$F.E.V._{\cdot 0\cdot 75}$ (litres)	V.C. (litres)	F.E.V. %
Non-miners	35–44	117·7	2·94	4·07	72·7
	45–54	105·0	2·63	3·78	69·8
	55–64	86·6*	2·17	3·30	65·4
Miners and ex-miners	35–44	109·9	2·75	3·95	68·6
	45–54	86·7	2·17	3·28	64·3
	55–64	75·0	1·88	2·89	63·4

* One man excluded.

Prevalence of Pneumoconiosis.—Table 3 shows the prevalence of pneumoconiosis (International Labour Organization, 1953) in each age group in the sample. Categories of simple pneumoconiosis are given separately but all categories of progressive massive fibrosis (P.M.F.) have been combined. Our expectation of equal numbers of men with and without pneumoconiosis in each decade was not realized. In the 35 to 44 age group over half and in the two older age groups nearly three-quarters of the men had radiological changes. The change from the earlier findings (Cochrane *et al.*, 1956) is probably due partly to observer differences in film classification and partly to progression of simple pneumoconiosis during the past six years.

Ventilatory Capacity.—Mean values for the I.M.B.C., $F.E.V._{\cdot 0\cdot 75}$, V.C. and F.E.V.% are shown in Table 4. At all ages miners and ex-miners recorded lower values than non-miners. The differences in the I.M.B.C. are all highly significant ($p < 0\cdot 01$) but the differences in the F.E.V.% are significant only in the two younger age groups. This shows once again the fact, which we have observed previously, that the F.E.V.% is a less useful test than the $F.E.V._{\cdot 0\cdot 75}$ for discriminating between two groups. Only a small part of the difference in means is due to progressive massive fibrosis. If cases with P.M.F. are excluded, the difference in I.M.B.C. of 14 litres per minute in the 45 to 54 and of 10 litres per minute in the 55 to 64 age groups is still statistically significant ($p < 0\cdot 01$).

TABLE 5

MEAN INDIRECT M.B.C. IN MINERS AND EX-MINERS ACCORDING TO RADIOLOGICAL CATEGORY OF PNEUMOCONIOSIS

Age Group	Radiological Category	No.	I.M.B.C. (litres/min.)	F.E.V.$_{1\cdot0}$ (litres)	V.C. (litres)	F.E.V.$_{1\cdot0}$%
35–44	O	36	113·7	2·84	4·11	69·4
	Simple	42	112·0	2·80	4·00	70·1
	P.M.F.	8	82·0	2·05	3·63	57·4
45–54	O	27	85·3	2·13	3·35	62·4
	Simple	41	98·7	2·57	3·65	68·7
	P.M.F.	27	76·1	1·90	3·10	59·7
55–64	O	25	77·1	1·93	2·88	66·1
	Simple	40	76·5	1·91	2·90	63·5
	P.M.F.	20	73·2	1·78	2·79	63·4

TABLE 7

PREVALENCE OF RESPIRATORY SYMPTOMS AND "CHRONIC BRONCHITIS" ACCORDING TO AGE, SEX, AND OCCUPATION IN SAMPLE 1958

Occupation	Age Group	No.	Cough	Sputum	Cough and Sputum	Chest Illness			Breathlessness		"Chronic Bronchitis"
						Once	More than Once	Total	Grade 2 and Over	Grade 3 and Over	
Non-miners	35–44	88	33 (37·5)	30 (34·1)	23 (26·1)	7 (8·0)	2 (2·3)	9 (10·2)	5 (5·7)	3 (3·4)	4 (4·5)
	45–54	88	31 (35·2)	27 (30·7)	21 (23·9)	8 (9·1)	8 (9·1)	16 (18·2)	14 (15·9)	8 (9·1)	11 (12·5)
	55–64	90	36 (40·0)	30 (33·3)	25 (27·8)	7 (7·8)	10 (11·1)	17 (18·9)	20 (22·2)	9 (10·0)	9 (10·0)
Miners and ex-miners	35–44	86	47 (54·7)	44 (51·2)	34 (39·5)	7 (8·1)	15 (17·4)	22 (25·6)	32 (37·2)	11 (12·8)	16 (18·6)
	45–54	95	58 (61·1)	63 (66·3)	51 (53·7)	10 (10·5)	26 (27·4)	36 (37·9)	49 (51·6)	22 (23·2)	33 (34·7)
	55–64	98	60 (61·2)	60 (61·2)	51 (52·0)	15 (15·3)	32 (32·7)	47 (48·0)	68 (69·4)	35 (35·7)	30 (31·9)
Women	55–64	171	27 (15·8)	28 (16·2)	17 (9·8)	24 (13·9)	15 (8·7)	39 (22·5)	61 (35·5)	27 (15·8)	12 (6·9)

A follow-up study of a random sample of men and women from Wales and Scotland surveyed in 1958 was carried out in 1961–63. The prevalence of respiratory symptoms and ventilatory capacity in 90% of a random sample of 600 men between the ages of 35 and 64 and 200 women between 55 and 64 living in the Rhondda Fach was carried out. The sample of men was stratified by age and occupation, 100 miners and ex-miners, and 100 non-miners being studied in each decade.

The higher prevalence of symptoms and lower mean indirect maximum breathing capacity (I.M.B.C.) of the miners and ex-miners, observed previously, was confirmed and within the mining group there was little relation of symptoms to radiological category of pneumoconiosis. Miners and ex-miners with progressive massive fibrosis had a lower mean I.M.B.C. than the rest at all ages.

Analysis of symptoms and I.M.B.C. by length of time spent working on the coal-getting shift in both miners and ex-miners did not suggest that the total dust dosage to which a man had been exposed during his working life was closely related to chronic respiratory disease. A lower prevalence of symptoms and a higher mean indirect M.B.C. was found in those who had worked for under one year on the coal-getting shift. Above one year no clear pattern of symptom prevalence was discerned although there was a slight downward trend in the mean indirect M.B.C. with increased time spent working on the coal-getting shift. When working miners alone were considered the reduction in ventilatory function with increasing duration of work was slightly greater.

Dust exposure alone seemed unlikely to account for all the excess respiratory disease in miners compared with the rest of the community and other possible explanations are discussed.

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Smoking was associated with an increased prevalence of symptoms and lower indirect M.B.C. in the men but not in the women. Differences in smoking habits could not, however, account for the differences between miners and non-miners, as these remained after standardization for smoking.

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In order to investigate further the high S.M.R. from bronchitis of miners' wives, to which the Registrar-General has alluded in his last two Decennial Mortality Supplements (Registrar-General, 1938 and 1958) we included a random sample of 200 women between the ages of 55 and 64. The number of men and women living in the area, the number sampled, the response rate, and number finally analysed are shown in Table 1.

Methods and Procedure.—The methods and procedure were similar to those used previously (Higgins and Cochran, 1958). Respiratory symptoms were recorded using a questionnaire comparable with that used on all previous surveys except the Rhondda investigation of 1954 already mentioned (Higgins *et al.*, 1956; 1959). The questionnaire was essentially the same as that recently approved by the Medical Research Council's Bronchitis Committee. Occupational histories from the time of leaving school and domiciliary histories from birth were obtained. The 0·75 second forced expiratory volume ($F.E.V._{\cdot 0\cdot 75}$) was measured and expressed as the indirect maximum breathing capacity (I.M.B.C.) by multiplying by 40 (McKerrow, McDermott, and Gilson, 1960). Standing and sitting heights and weights were measured and a postero-anterior chest radiograph was taken.

Members of the sample were visited in their homes and asked to participate in the investigation. Appointments were made and transport to and from the hall where the tests were carried out was offered.

Results

Table 2 shows the mean ages and main measurements in each group. The decline in mean height with age noted previously in the Vale of Glamorgan (Higgins, 1957) is again seen. The miners and ex-miners over 45 years were on the average significantly shorter and at all ages lighter than the corresponding non-miners. The mean heights of the non-miners are half to one inch above those found in the survey of the population of Great Britain carried out by the Ministry of Food (Kemsley, 1950) in 1943.

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RANDOM SAMPLE STRATIFIED BY AGE AND OCCUPATION

Occupation	Age Group	No. in Population at Census*	No. Sampled	Dead	Left Area	Refused	Not Seen	Seen	Excluded†	Added from Other Groups	Finally Analysed
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	45–54	338	100	1	2	8	1	88	3	3	88
	55–64	146	100	0	0	9	2	89	4	1	86
Miners and ex-miners	35–44	1,127	100	0	2	8	0	90	4	0	86
	45–54	1,283	100	0	0	5	0	95	3	3	95
	55–64	1,114	100	3	0	4	1	92	1	3	94
Women	55–64	1,535	200	4	1	12	8	175	2	0	173

* Date of Census June 1, 1958.

† Because age or occupational history was found to be incorrect.

TABLE 2

MEAN AGE AND MEASUREMENTS

Occupation	Age Group	No.	Age (years)	Standing Height		Sitting Height		Weight	
				in.	cm.	in.	cm.	lb.	kg.
Non-miners	35–44	88	39·5	67·1	170·4	35·3	89·7	154·7	70·2
	45–54	88	49·7	66·7	169·4	35·1	89·2	154·6	70·1
	55–64	86	59·4	66·4	168·7	34·4	87·4	148·0	67·1
Miners and ex-miners	35–44	86	40·1	67·0	170·2	35·4	89·9	147·7	67·0
	45–54	95	49·5	65·9	167·4	34·7	88·1	144·2	65·4
	55–64	94	59·9	65·5	166·4	34·1	86·6	140·1	63·5
Women	55–64	173	59·7	60·9	154·7	32·2	81·8	145·3	65·9

TABLE 3

PREVALENCE OF PNEUMOCONIOSIS IN THE RHONDDA FACH MINERS AND EX-MINERS IN SAMPLE 1958

Age Group	Radiological Category						Total
	0	1	2	3	All Simple Pneumoconiosis	P.M.F.	
35–44	36 (41·9)	18 (20·9)	13 (15·1)	11 (12·8)	42 (48·8)	8 (9·3)	86 (100·0)
45–54	27 (28·4)	18 (18·9)	12 (12·6)	11 (11·6)	41 (43·2)	27 (28·4)	95 (100·0)
55–64	25 (26·6)	24 (25·5)	15 (16·0)	1 (1·1)	40 (42·6)	29 (30·9)	94 (100·1)

Percentages are given in brackets.

TABLE 4

MEAN VENTILATORY CAPACITY MEASUREMENTS IN NON-MINERS, MINERS, AND EX-MINERS ACCORDING TO AGE

Occupation	Age Group	I.M.B.C. (litres/min.)	$F.E.V._{0·75}$ (litres)	V.C. (litres)	F.E.V. %
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	45–54	105·0	2·63	3·78	69·8
	55–64	86·6*	2·17	3·30	65·4
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* One man excluded.

Prevalence of Pneumoconiosis.—Table 3 shows the prevalence of pneumoconiosis (International Labour Organization, 1953) in each age group in the sample. Categories of simple pneumoconiosis are given separately but all categories of progressive massive fibrosis (P.M.F.) have been combined. Our expectation of equal numbers of men with and without pneumoconiosis in each decade was not realized. In the 35 to 44 age group over half and in the two older age groups nearly three-quarters of the men had radiological changes. The change from the earlier findings (Cochrane *et al.*, 1956) is probably due partly to observer differences in film classification and partly to progression of simple pneumoconiosis during the past six years.

Ventilatory Capacity.—Mean values for the I.M.B.C., $F.E.V._{0·75}$, V.C. and F.E.V.% are shown in Table 4. At all ages miners and ex-miners recorded lower values than non-miners. The differences in the I.M.B.C. are all highly significant ($p < 0·01$) but the differences in the F.E.V.% are significant only in the two younger age groups. This shows once again the fact, which we have observed previously, that the F.E.V.% is a less useful test than the $F.E.V._{0·75}$ for discriminating between two groups. Only a small part of the difference in means is due to progressive massive fibrosis. If cases with P.M.F. are excluded, the difference in I.M.B.C. of 14 litres per minute in the 45 to 54 and of 10 litres per minute in the 55 to 64 age groups is still statistically significant ($p < 0·01$).

TABLE 5

MEAN INDIRECT M.B.C. IN MINERS AND EX-MINERS ACCORDING TO RADIOLOGICAL CATEGORY OF PNEUMOCONIOSIS

Age Group	Radiological Category	No.	I.M.B.C. (litres/min.)	F.E.V.$_{0\cdot75}$ (litres)	V.C. (litres)	F.E.V.%
35–44	0	36	113·7	2·84	4·11	69·4
	Simple	42	112·0	2·80	4·00	70·1
	P.M.F.	8	82·0	2·05	3·03	57·4
45–54	0	27	85·3	2·13	3·35	62·4
	Simple	41	94·7	2·37	3·45	68·7
	P.M.F.	27	76·1	1·90	3·10	59·7
55–64	0	25	77·1	1·93	2·88	66·1
	Simple	40	76·5	1·91	2·90	61·5
	P.M.F.	29	71·2	1·78	2·79	63·4

While at all ages P.M.F. was associated with a significant reduction in the mean I.M.B.C. at no age did miners with simple pneumoconiosis have significantly lower values than those without (Table 5). Outside this Unit the F.E.V. is usually measured over one second. The correlation between the 0·75 second and 1 second tests is however very high ($r = 0{\cdot}998$) and the F.E.V.$_{1\cdot0}$ may be readily obtained from the regression

$$\text{F.E.V.}_{1\cdot0} = 1{\cdot}08\ \text{F.E.V.}_{0\cdot75} + 0{\cdot}09 \text{ (litres)}$$

(McKerrow *et al.*, 1960).

Table 6 compares I.M.B.C., F.E.V.$_{0\cdot75}$ and F.E.V.$_{1\cdot0}$.

TABLE 6

RELATION BETWEEN INDIRECT M.B.C., F.E.V.$_{0\cdot75}$, AND F.E.V.$_{1\cdot0}$

I.M.B.C. (litres/min.)	F.E.V.$_{0\cdot75}$ (litres)	F.E.V.$_{1\cdot0}$ (litres)
10	0·25	0·36
20	0·50	0·63
30	0·75	0·90
40	1·00	1·17
50	1·25	1·44
60	1·50	1·71
70	1·75	1·98
80	2·00	2·25
90	2·25	2·52
100	2·50	2·79
110	2·75	3·06
120	3·00	3·33
130	3·25	3·60
140	3·50	3·87
150	3·75	4·14
160	4·00	4·41
170	4·25	4·68
180	4·50	4·95
190	4·75	5·22
200	5·00	5·49

Based on regression:

F.E.V.$_{1\cdot0}$ = 1.08 F.E.V.$_{0\cdot75}$ + 0·09 (litres) (McKerrow *et al.*, 1960)

Prevalence of Respiratory Symptoms.—Tables 7 and 8 compare the prevalence of the main symptoms in miners and ex-miners and non-miners and within the mining group according to radiological category of pneumoconiosis. At all ages the miners had between two and three times as high a prevalence of each symptom as the non-miners; but within the mining group symptom prevalence is not closely related to radiological category and no consistent pattern emerges. Men with P.M.F. had a slightly higher prevalence of breathlessness at all ages and rather more chest illness and "chronic bronchitis" in the 35 to 44 and 45 to 54 age groups, but not in the 55 to 64 age groups. Miners and ex-miners with simple pneumoconiosis tended to have a higher prevalence of cough and sputum than those without in the 35 to 44 and 55 to 64, but not in the 45 to 54, age groups.

The lower prevalence of all symptoms among the women (Table 9) compared with the appropriate non-mining males, is in line with expectation. The prevalence recorded was however generally higher than that found in the Vale of Glamorgan (Higgins, 1957) and in Annandale (Higgins and Cochran, 1958) and this difference is such as one might expect between town and country.

The prevalence of symptoms and mean I.M.B.C. in the women according to the occupation of their husbands is also shown in Table 9. Wives of miners and ex-miners recorded a higher prevalence of symptoms and a lower ventilatory capacity than the wives of non-miners. It is difficult to draw any far-reaching conclusion from this finding, since there were social class differences between the two groups, for which, with so few non-miners' wives, it was not possible to standardize.

Aetiological Factors

Mining and Dust Exposure.—We have tried to assess the importance of mining and coal dust exposure by relating respiratory symptoms and the indirect M.B.C. to the length of time spent working on the coal-getting shift (Tables 10 and 11). In the Tables concerned with the indirect M.B.C. the radiological categories of pneumoconiosis are shown separately; but in dealing with the pre-

TABLE 7

PREVALENCE OF RESPIRATORY SYMPTOMS AND "CHRONIC BRONCHITIS" ACCORDING TO AGE, SEX, AND OCCUPATION IN SAMPLE 1958

Occupation	Age Group	No.	Cough	Sputum	Cough and Sputum	Chest Illness			Breathlessness		"Chronic Bronchitis"*
						Once	More than Once	Total	Grade 2 and Over	Grade 3 and Over	
Non-miners	35–44	88	33 (37·5)	30 (34·1)	23 (26·1)	7 (8·0)	2 (2·3)	9 (10·2)	5 (5·7)	3 (3·4)	4 (4·5)
	45–54	88	31 (35·2)	27 (30·7)	21 (23·9)	6 (6·8)	8 (9·1)	14 (15·9)	14 (15·9)	6 (6·8)	11 (12·5)
	55–64	86	36 (41·9)	30 (34·8)	25 (29·1)	7 (8·1)	10 (11·6)	17 (19·8)	20 (23·3)	9 (10·5)	9 (10·5)
Miners and ex-miners	35–44	86	47 (54·7)	44 (51·2)	34 (39·5)	7 (8·1)	15 (17·4)	22 (25·6)	32 (37·2)	11 (12·8)	16 (18·6)
	45–54	95	58 (61·1)	61 (64·2)	51 (53·7)	10 (10·5)	26 (27·4)	36 (37·9)	49 (51·6)	22 (23·2)	33 (34·7)
	55–64	94	60 (63·8)	60 (63·8)	53 (56·4)	13 (13·8)	22 (23·4)	35 (37·2)	61 (64·9)	35 (37·2)	30 (31·9)
Women	55–64	173	27 (15·6)	28 (16·2)	17 (9·8)	24 (13·9)	15 (8·7)	39 (22·5)	61 (35·3)	27 (15·6)	12 (6·9)

Percentages in brackets.
*Defined as persistent sputum and at least one chest illness sufficiently severe to keep a man off work for one week during past three years.

TABLE 8

PREVALENCE OF RESPIRATORY SYMPTOMS AND "CHRONIC BRONCHITIS" IN MINERS ACCORDING TO RADIOLOGICAL CATEGORY OF PNEUMOCONIOSIS

Age Group	Radiological Category of Pneumoconiosis	No.	Cough	Sputum	Cough and Sputum	Chest Illness			Breathlessness		"Chronic Bronchitis"
						Once	More than Once	Total	Grade 2 and Over	Grade 3 and Over	
35–44	0	36	16 (44·4)	16 (44·4)	12 (33·3)	4 (11·1)	3 (8·3)	7 (19·4)	8 (22·2)	4 (11·1)	5 (13·9)
	1, 2, 3 S.P.*	42	26 (61·9)	24 (57·1)	18 (42·9)	2 (4·8)	10 (23·8)	12 (28·6)	18 (42·9)	5 (11·9)	9 (21·4)
	P.M.F.	8	5 (62·5)	4 (50·0)	4 (50·0)	1 (12·5)	2 (25·0)	3 (37·5)	6 (75·0)	2 (25·0)	2 (25·0)
45–54	0	27	18 (66·7)	15 (55·6)	15 (55·6)	3 (11·1)	8 (29·6)	11 (40·7)	12 (44·4)	8 (29·6)	9 (33·3)
	1, 2, 3 S.P.	41	23 (56·1)	27 (65·9)	21 (51·2)	2 (4·9)	8 (19·5)	10 (24·4)	18 (43·9)	6 (14·6)	10 (24·4)
	P.M.F.	27	17 (63·0)	19 (70·4)	15 (55·6)	5 (18·5)	10 (37·0)	15 (55·6)	19 (70·4)	8 (29·6)	14 (51·9)
55–64	0	25	14 (56·0)	16 (64·0)	12 (48·0)	3 (12·0)	7 (28·0)	10 (40·0)	14 (56·0)	8 (32·0)	9 (36·0)
	1, 2, 3 S.P.	40	28 (70·0)	28 (70·0)	26 (65·0)	7 (17·5)	8 (20·0)	15 (37·5)	26 (65·0)	14 (35·0)	12 (30·0)
	P.M.F.	29	18 (62·1)	16 (55·2)	15 (51·7)	3 (10·3)	7 (24·1)	10 (34·5)	21 (72·4)	13 (44·8)	9 (31·0)

* Simple pneumoconiosis.
Percentages in brackets.

TABLE 9

PREVALENCE OF RESPIRATORY SYMPTOMS AND MEAN I.M.B.C. OF WOMEN ACCORDING TO MARITAL STATUS AND OCCUPATION OF HUSBAND

Group	No.	Cough	Sputum	Cough and Sputum	Chest Illness			Breathlessness		"Chronic Bronchitis"	Mean I.M.B.C. (litres/min.)
					Once	More than Once	Total	Grade 2 and Over	Grade 3 and Over		
Spinsters	10	1	2	1	1	1	2	1	1	2	56·6
Wives of non-miners	28	0 (—)	2 (7·1)	0 (—)	2 (7·1)	1 (3·6)	3 (10·7)	4 (14·2	1 (3·6)	0 (—)	68·6
Wives of miners and ex-miners	135	26 (19·3)	24 (17·8)	16 (11·9)	21 (15·6)	13 (9·6)	34 (25·2)	56 (41·5)	25 (18·5)	10 (7·4)	60·5
All women	173	27 (15·6)	28 (16·2)	17 (9·8)	24 (13·9)	15 (8·7)	39 (22·5)	61 (35·3)	27 (15·6)	12 (6·9)	61·6

Percentages in brackets.

valence of symptoms this is not possible due to the small numbers. A somewhat higher prevalence of symptoms was observed in those who had worked for more than one year either underground or on the coal-face; but over one year there was no consistent increase in prevalence with increased duration. Similarly the mean I.M.B.C. was higher in those who had worked less than one year, the values closely approximating to those expected for non-miners. There also appears to be an overall downward trend (which does not however reach the 5% level of statistical significance) in the mean

TABLE 10

PREVALENCE OF SYMPTOMS ACCORDING TO NUMBER OF YEARS SPENT WORKING ON THE COAL-GETTING SHIFT

Age Group		Years Spent on Coal-getting Shift					
		0–1	1–9	10–19	20–29	30+	Total
35–44	No. in group	16	46	18	6		86
	No. with:						
	Cough and sputum	6 (37·5)	18 (39·1)	9 (50·0)	1 (16·7)		34
	Chest illness	2 (12·5)	13 (28·3)	6 (33·3)	1 (16·7)		22
	Breathlessness	2 (12·5)	18 (39·1)	9 (50·0)	3 (50·0)		32
	"Chronic bronchitis"	1 (6·3)	12 (26·1)	2 (11·1)	1 (16·7)		16
45–54	No. in group	6	38	23	25	3	95
	No. with:						
	Cough and sputum	3 (50·0)	18 (47·4)	15 (65·2)	12 (48·0)	3 (100·0)	51
	Chest illness	0	16 (42·1)	12 (52·2)	7 (28·0)	1 (33·3)	36
	Breathlessness	1 (16·7)	22 (57·9)	12 (52·2)	12 (48·0)	2 (66·7)	49
	"Chronic bronchitis"	0	14 (36·8)	11 (47·8)	7 (28·0)	1 (33·3)	33
55–64	No. in group	10	33	28	17	6	94
	No. with:						
	Cough and sputum	4 (40·0)	17 (51·5)	17 (60·7)	11 (64·7)	4 (66·7)	53
	Chest illness	2 (20·0)	14 (42·4)	11 (39·3)	7 (41·2)	1 (16·7)	35
	Breathlessness	4 (40·0)	22 (66·7)	18 (64·3)	13 (76·4)	4 (66·7)	61
	"Chronic bronchitis"	1 (10·0)	12 (36·4)	9 (32·1)	7 (41·2)	1 (16·7)	30

TABLE 11

MEAN I.M.B.C. ACCORDING TO NUMBER OF YEARS SPENT WORKING ON COAL-GETTING SHIFT

Age Group	Radiological Category of Pneumoconiosis	Years Spent on Coal-getting Shift							
		< 1		1–9		10–19		20 and over	
		No.	I.M.B.C.	No.	I.M.B.C.	No.	I.M.B.C.	No.	I.M.B.C.
35–44	0	16	112·3	19	115·1	1	109·0	0	—
	1, 2, 3			25	114·0	11	112·9	6	102·2
	P.M.F.			2	78·0	6	83·3	0	—
	All	16	112·3	46	112·9	18	102·8	6	102·2
45–54	0	6	111·8	15	78·2	4	76·0	2	78·0
	1, 2, 3			18	96·0	11	98·1	12	89·5
	P.M.F.			5	92·8	8	61·0	14	78·8
	All	6	111·8	38	88·6	23	81·3	28	83·3
55–64	0	3	92·3	16	79·8	3	43·3	3	81·7
	1, 2, 3	5	95·2	13	71·2	18	79·7	4	56·0
	P.M.F.	2	71·5	4	71·5	7	66·6	16	73·1
	All	10	89·5	33	75·4	28	72·5	23	71·3

I.M.B.C. with time spent on the coal-getting shift. The analysis by radiological category of pneumoconiosis suggests that this is more obvious in the men without pneumoconiosis and in those with P.M.F. and that it does not occur in those with simple pneumoconiosis. This is in line with other observations (Cochrane and Higgins, 1961) and might possibly be explained in part by the loss of cases of simple pneumoconiosis with lower I.M.B.C.'s into the P.M.F. group.

If inhaling coal-mine dust does depress lung function we might expect improvement to occur when a man leaves mining and is no longer exposed to coal dust. By including ex-miners in our analysis we might possibly have concealed some of the effect of the dust dose. We have therefore repeated the analysis for miners and ex-miners separately (Table 12). This certainly suggests, at least in the 55 to 64 age group, that the decline in ventilatory capacity with increasing years spent working on the coal-face is greater in the working miners and therefore supports Worth, Gasthaus, Lühning, Muysers, Siehoff, and Werner (1959) who showed a fall in ventilatory function with duration of underground work in a large group of working miners from the left lower Rhine. A decline in lung function with increasing time spent working underground was also recorded in miners attending hospital by Carstens, Brinkmann, Lange, Meisterernst, and Schlicht (1958).

Tobacco Smoking.—Smoking habits were recorded as in our previous studies in the way originally advocated by Doll and Bradford Hill (1950). The current smoking groups were then combined into light (1-14 g. tobacco per day) and heavy (15 g. and over per day). The results for the three age groups when analysed separately indicated a similar conclusion to that found when they were combined. For simplicity and brevity therefore Table 13 shows the analysis for all ages.

There was a higher proportion of non-smokers among the non-miners and more of the miners and ex-miners were light smokers. These findings support previous observations (Cross, McDowell, and Posner, 1958). Differences in prevalence of respiratory symptoms and I.M.B.C. between miners and non-miners are still obvious after standardizing for tobacco smoking. With the exception of breathlessness, current smokers had a higher prevalence of symptoms than either non-smokers or ex-smokers. This is more obvious in the mining group. The non-smokers recorded a higher mean I.M.B.C. than the smokers and ex-smokers, though in the case of the mining group the difference is not large. These findings in regard to tobacco smoking are in agreement with previous results in other areas but are rather less striking than our observations in Staveley.

Among the women the prevalence of symptoms was higher in smokers than in non-smokers; but

TABLE 12

MEAN I.M.B.C. ACCORDING TO NUMBER OF YEARS SPENT WORKING ON COAL-GETTING SHIFT

Age	Occupation	Years Spent on Coal-getting Shift										Total	
		< 1		1–9		10–19		20–29		30 and over			
		No	I.M.B.C.	No.	I.M.B.C.	No.	I.M.B.C.	No.	I.M.B.C.	No.	I.M.B.C.	No.	I.M.B.C.
35–44	Miners	12	111·2	23	119·0	10	105·9	6	102·2	0	—	51	112·6
	Ex-miners	4	115·8	23	106·8	8	99·0	0	—	0	—	35	106·0
	Both	16	112·3	46	112·9	18	102·8	6	102·2	0	—	86	109·9
45–54	Miners	4	119·8	17	94·8	11	91·9	18	87·2	1	112·0	50	94·1
	Ex-miners	2	96·0	21	83·5	12	71·7	7	78·1	2	52·0	45	78·6
	Both	6	111·8	38	88·6	23	81·3	25	84·7	3	72·0	95	86·7
55–64	Miners	5	92·2	12	81·4	9	70·7	8	64·6	3	71·0	37	75·8
	Ex-miners	5	87·0	21	72·0	19	73·4	9	73·2	3	83·3	57	74·6
	Both	10	89·6	23	75·4	28	72·5	17	69·2	6	77·2	94	75·0

TABLE 13

PREVALENCE OF SYMPTOMS AND MEAN I.M.B.C. ACCORDING TO SMOKING HABITS IN MEN OF ALL AGES

Occupation		Non-smokers	Smokers		Ex-smokers	Total
			Light (1–14 g./day)	Heavy (15 g./day and over)		
Non-miners	Number	33 (12·6)	94 (35·9)	97 (37·0)	38 (14·5)	262 (100·0)
	Those with:					
	Persistent cough and sputum	5 (15·2)	19 (20·2)	41 (42·3)	4 (10·5)	
	Chest illness	4 (12·2)	14 (14·9)	15 (15·5)	7 (18·4)	
	Breathlessness (Grade 2 and over)	5 (15·2)	11 (11·7)	17 (17·5)	6 (15·7)	
	" Chronic bronchitis "	3 (9·1)	9 (9·6)	8 (8·2)	4 (10·5)	
	Mean M.B.C.	114·6	104·1	99·4	105·9	
Miners and ex-miners	Number	15 (5·5)	135 (49·1)	82 (29·8)	43 (15·6)	275 (100·0)
	Those with:					
	Persistent cough and sputum	3 (20·0)	71 (52·6)	51 (62·2)	13 (30·2)	
	Chest illness	4 (26·7)	47 (34·8)	32 (39·0)	10 (23·3)	
	Breathlessness (Grade 2 and over)	7 (46·7)	73 (54·1)	39 (47·6)	23 (53·5)	
	" Chronic bronchitis "	2 (13·3)	42 (31·1)	28 (34·1)	7 (16·3)	
	Mean M.B.C.	93·1	89·0	88·3	93·6	

Percentages are in brackets.

TABLE 10

PREVALENCE OF SYMPTOMS ACCORDING TO NUMBER OF YEARS SPENT WORKING ON THE COAL-GETTING SHIFT

Age Group		Years Spent on Coal-getting Shift					
		0–1	1–9	10–19	20–29	30+	Total
35–44	No. in group	16	46	18	6		86
	No. with:						
	Cough and sputum	6 (37·5)	18 (39·1)	9 (50·0)	1 (16·7)		34
	Chest illness	2 (12·5)	13 (28·3)	6 (33·3)	1 (16·7)		22
	Breathlessness	2 (12·5)	18 (39·1)	9 (50·0)	3 (50·0)		32
	" Chronic bronchitis"	1 (6·3)	12 (26·1)	2 (11·1)	1 (16·7)		16
45–54	No. in group	6	38	23	25	3	95
	No. with:						
	Cough and sputum	3 (50·0)	18 (47·4)	15 (65·2)	12 (48·0)	3 (100·0)	51
	Chest illness	0	16 (42·1)	12 (52·2)	7 (28·0)	1 (33·3)	36
	Breathlessness	1 (16·7)	22 (57·9)	12 (52·2)	12 (48·0)	2 (66·7)	49
	" Chronic bronchitis "	0	14 (36·8)	11 (47·8)	7 (28·0)	1 (33·3)	33
55–64	No. in group	10	33	28	17	6	94
	No. with:						
	Cough and sputum	4 (40·0)	17 (51·5)	17 (60·7)	11 (64·7)	4 (66·7)	53
	Chest illness	2 (20·0)	14 (42·4)	11 (39·3)	7 (41·2)	1 (16·7)	35
	Breathlessness	4 (40·0)	22 (66·7)	18 (64·3)	13 (76·4)	4 (66·7)	61
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Age Group	Radiological Category of Pneumoconiosis	Years Spent on Coal-getting Shift							
		< 1		1–9		10–19		20 and over	
		No.	I.M.B.C.	No.	I.M.B.C.	No.	I.M.B.C.	No.	I.M.B.C.
35–44	0	16	112·3	19	115·1	1	109·0	0	—
	1, 2, 3			25	114·0	11	112·9	6	102·2
	P.M.F.			2	78·0	6	83·3	0	—
	All	16	112·3	46	112·9	18	102·8	6	102·2
45–54	0	6	111·8	15	78·2	4	76·0	2	78·0
	1, 2, 3			18	96·0	11	98·1	12	89·5
	P.M.F.			5	92·8	8	61·0	14	78·8
	All	6	111·8	38	88·6	23	81·3	28	83·3
55–64	0	3	92·3	16	79·8	3	43·3	3	81·7
	1, 2, 3	5	95·2	13	71·2	18	79·7	4	56·0
	P.M.F.	2	71·5	4	71·5	7	66·6	16	73·1
	All	10	89·5	33	75·4	28	72·5	23	71·3

I.M.B.C. with time spent on the coal-getting shift. The analysis by radiological category of pneumoconiosis suggests that this is more obvious in the men without pneumoconiosis and in those with P.M.F. and that it does not occur in those with simple pneumoconiosis. This is in line with other observations (Cochrane and Higgins, 1961) and might possibly be explained in part by the loss of cases of simple pneumoconiosis with lower I.M.B.C.'s into the P.M.F. group.

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Among the women the prevalence of symptoms was higher in smokers than in non-smokers; but

TABLE 12

MEAN I.M.B.C. ACCORDING TO NUMBER OF YEARS SPENT WORKING ON COAL-GETTING SHIFT

Age	Occupation	Years Spent on Coal-getting Shift										Total	
		< 1		1–9		10–19		20–29		30 and over			
		No	I.M.B.C.	No.	I.M.B.C.	No.	I.M.B.C.	No.	I.M.B.C.	No.	I.M.B.C.	No.	I.M.B.C.
35–44	Miners	12	111·2	23	119·0	10	105·9	6	102·2	0	—	51	112·6
	Ex-miners	4	115·8	23	106·8	8	99·0	0	—	0	—	35	106·0
	Both	16	112·3	46	112·9	18	102·8	6	102·2	0	—	86	109·9
45–54	Miners	4	119·8	17	94·8	11	91·9	18	87·2	1	112·0	50	94·1
	Ex-miners	2	96·0	21	83·5	12	71·7	7	78·1	2	52·0	45	78·6
	Both	6	111·8	38	88·6	23	81·3	25	84·7	3	72·0	95	86·7
55–64	Miners	5	92·2	12	81·4	9	70·7	8	64·6	3	71·0	37	75·8
	Ex-miners	5	87·0	21	72·0	19	73·4	9	73·2	3	83·3	57	74·6
	Both	10	89·6	23	75·4	28	72·5	17	69·2	6	77·2	94	75·0

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Occupation		Non-smokers	Smokers		Ex-smokers	Total
			Light (1–14 g./day)	Heavy (15 g./day and over)		
Non-miners	Number	33 (12·6)	94 (35·9)	97 (37·0)	38 (14·5)	262 (100·0)
	Those with:					
	Persistent cough and sputum	5 (15·2)	19 (20·2)	41 (42·3)	4 (10·5)	
	Chest illness	4 (12·2)	14 (14·9)	15 (15·5)	7 (18·4)	
	Breathlessness (Grade 2 and over)	5 (15·2)	11 (11·7)	17 (17·5)	6 (15·7)	
	" Chronic bronchitis "	3 (9·1)	9 (9·6)	8 (8·2)	4 (10·5)	
	Mean M.B.C.	114·6	104·1	99·4	105·9	
Miners and ex-miners	Number	15 (5·5)	135 (49·1)	82 (29·8)	43 (15·6)	275 (100·0)
	Those with:					
	Persistent cough and sputum	3 (20·0)	71 (52·6)	51 (62·2)	13 (30·2)	
	Chest illness	4 (26·7)	47 (34·8)	32 (39·0)	10 (23·3)	
	Breathlessness (Grade 2 and over)	7 (46·7)	73 (54·1)	39 (47·6)	23 (53·5)	
	" Chronic bronchitis "	2 (13·3)	42 (31·1)	28 (34·1)	7 (16·3)	
	Mean M.B.C.	93·1	89·0	88·3	93·6	

Percentages are in brackets.

smokers recorded a higher mean I.M.B.C. (Table 14). A possible explanation of this anomalous finding might be that women with high I.M.B.C. values are more likely to take up smoking.

Discussion

The present findings support our earlier observations in the Rhondda Fach (Carpenter *et al.*, 1956; Cochrane, 1958; Higgins, 1960) that miners and ex-miners living there have more chronic non-specific respiratory disease than non-miners. Similar findings in Leigh and Staveley (Higgins *et al.*, 1956; 1959) together with the national mortality rates (Registrar-General, 1958) permit the conclusion that this excess of respiratory disease is general among the mining community.

In our earlier study in the Rhondda we compared the ventilatory capacity of miners and ex-miners without pneumoconiosis with those with Category 3 simple pneumoconiosis. We found little difference in mean I.M.B.C. between the two groups in men in the 25 to 34 age group, but in the 55 to 64 age group miners and ex-miners without pneumoconiosis recorded a lower mean I.M.B.C. than the men with Category 3 simple pneumoconiosis and this lower value was associated with a bimodal frequency distribution. The difference between the two groups however did not quite reach the 5% significance level and we were uncertain of the true meaning of the finding. As there was no significant difference in mean I.M.B.C. between those with and those without simple pneumoconiosis in this survey, it is likely that the earlier finding was due to sampling error rather than to the existence of a cohort, in which the proportion of disabled men was unduly high.

TABLE 14

PREVALENCE OF SYMPTOMS AND MEAN I.M.B.C ACCORDING TO SMOKING HABITS IN WOMEN AGED 55 TO 64

	Non-smokers	Smokers		Ex-smokers
		Light (1–14 g./day)	Heavy (15 g./day and over)	
Number	141	27	2	3
Those with:				
Persistent cough and sputum	9 (6·4)	6 (22·2)	1	1
Chest illness	30 (21·3)	8 (29·6)	1	0
Breathlessness (Grade 2 and over)	51 (36·2)	9 (33·3)	1	0
" Chronic bronchitis "	8 (5·7)	3 (11·1)	1	0
Mean I.M.B.C.	50·6	59·0	76·5	88·3

Percentages are in brackets.

TABLE 15

PREVALENCE OF RESPIRATORY SYMPTOMS AND MEAN I.M.B.C. IN MEN AGED 55–64 IN RANDOM SAMPLES OF THE POPULATION

Area	Rural Denmark	Rural Scotland and Wales		Urban England and Wales										
	Bornholm*	Annandale	Vale of Glamorgan	Leigh			Staveley					Rhondda Fach		
Occupation	Non-dusty	Non-dusty	Non-dusty	Non-miners	Miners and Ex-miners		Non-dusty	Miners and Ex-miners		Foundry and Ex-foundry Workers		Non-miners	Miners and Ex-miners	
Radiological Category					0	Simple Pneumoconiosis		0	Simple Pneumoconiosis	0	Simple Pneumoconiosis		0	Simple Pneumoconiosis
No. in sample	156	87	86	84	101	21	81	96	53	50	14	86	25	40
No. with:														
Persistent cough and sputum	14 (9·0)	17 (19·5)	22 (25·6)	15 (17·9)	38 (37·6)	4 (19·0)	26 (32·1)	38 (39·6)	20 (37·7)	15 (30·0)	5 (35·7)	25 (29·1)	12 (48·0)	26 (65·0)
Chest illness														
Once	10 (6·4)	12 (13·8)	10 (11·6)	6 (7·1)	9 (8·9)	3 (14·3)	7 (8·6)	12 (12·5)	2 (3·8)	4 (8·0)	0 (—)	7 (8·1)	3 (12·0)	7 (17·5)
More than once	0 (—)	4 (4·6)	4 (4·7)	11 (13·1)	23 (22·8)	4 (19·0)	10 (12·3)	15 (15·6)	12 (22·6)	4 (8·0)	1 (7·1)	10 (11·6)	7 (28·0)	8 (20·0)
Total	10 (6·4)	16 (18·3)	14 (16·3)	17 (20·2)	32 (31·7)	7 (33·3)	17 (21·0)	27 (28·1)	14 (26·4)	8 (16·0)	1 (7·1)	17 (19·8)	10 (40·0)	15 (37·5)
Breathlessness														
Grades 2 and over	25 (16·0)	25 (28·7)	21 (24·4)	19 (22·6)	37 (36·6)	8 (38·1)	27 (33·3)	31 (32·3)	25 (47·2)	22 (44·0)	4 (28·6)	20 (23·3)	14 (56·0)	26 (65·0)
Grades 3 and over	7 (4·5)	8 (9·2)	7 (7·9)	6 (7·2)	25 (24·8)	2 (9·5)	9 (11·1)	8 (8·3)	9 (17·0)	7 (14·0)	2 (14·2)	9 (10·5)	8 (32·0)	14 (35·0)
" Chronic bronchitis "	4 (2·6)	6 (6·9)	5 (5·8)	9 (10·7)	27 (26·7)	3 (14·3)	12 (14·8)	18 (18·8)	13 (24·5)	5 (10·0)	0 (—)	9 (10·5)	9 (36·0)	12 (30·0)
Mean I.M.B.C.	106	95	89	85	76	85	90	87	87	85	82	87	77	77

Percentages are in brackets.
*Olsen and Gilson (1960).

TABLE 16

PREVALENCE OF RESPIRATORY SYMPTOMS AND I.M.B.C. ACCORDING TO LENGTH OF TIME SPENT ON COAL-GETTING SHIFT: MINERS AND EX-MINERS AGED 55–64 SEEN IN LEIGH

	Years Spent on Coal-getting Shift					
	1	1–9	10–19	20–29	30–39	40 +
All in the sample	40	18	33	28	10	3
Those with:						
Cough and sputum	10 (25·0)	5 (27·8)	16 (48·5)	12 (42·9)	3 (30·0)	0 (—)
Chest illness	13 (32·5)	5 (27·8)	9 (27·3)	12 (42·9)	3 (30·0)	0 (—)
Breathlessness	16 (40·0)	6 (33·3)	10 (30·3)	12 (42·9)	4 (40·0)	1 (33·3)
" Chronic bronchitis "	10 (25·0)	3 (16·7)	7 (21·2)	10 (35·7)	1 (10·0)	0 (—)
I.M.B.C.	78·9	79·8	80·4	69·3	75·2	87·7

Percentages are in brackets

Regional Differences.—One of the striking findings in our comparisons of miners and non-miners in different areas has been that there are considerable regional differences in the amount of chronic non-specific respiratory disease among miners. Table 15 shows that with the exception of persistent cough and sputum, which appeared surprisingly uncommon in Leigh, non-miners recorded a similar prevalence of symptoms and similar mean I.M.B.C. in each of the three areas. But whereas in Staveley the miners and ex-miners had only a slightly higher prevalence of symptoms and an insignificantly lower I.M.B.C. than the corresponding group of non-miners in the Rhondda Fach the differences between them were much greater.

Cause of the Occupational Difference.—We cannot attribute the difference in the amount of chronic respiratory disease between non-miners and miners and ex-miners to different degrees of exposure to general atmospheric pollution. For the miner, while working underground, is spared the vagaries of the British climate and so is less exposed to fog and " smog " than others. Nor do differences in tobacco consumption between miners and non-miners explain the finding. In Leigh the smoking habits of mining and non-mining groups were remarkably similar and in the present survey the occupational difference is still apparent after standardizing for tobacco consumption. Genetic differences leading to increased susceptibility, though of possible importance in the aetiology of bronchitis in general, are unlikely to affect only the miners.

Social class differences are however perhaps more important. The gradient in the mortality rates from bronchitis with social class has long been a striking feature of the national statistics. In the Rhondda Fach there are certainly differences in social class between the two occupational groups and these class differences are particularly evident in the older men, the professional classes being exceptionally highly represented among the non-miners. Exclusion of classes I and II from the non-miners does not however abolish the respiratory disease difference between them and the miners. The lower mean I.M.B.C. and higher prevalence of respiratory symptoms in the wives of miners and ex-miners provide some further support for a social factor accounting for some of the difference between miners and non-miners.

Exposure to dust at work is widely believed to be an important cause of bronchitis and it is surprising therefore how difficult it has proved in our surveys to show any very close relation between dust dosage and either symptom prevalence or lung function in all miners and ex-miners in the area. It is of course possible that the relation one might expect is concealed because those affected by dust move either to less dusty jobs within the industry or to jobs outside mining, with the result that those who have worked for the longer periods either undergound or on the coal-face will tend to be the fitter survivors. It is interesting in this connexion that Becklake, Zwi, and Lutz (1959) found no relationship between respiratory symptoms and dust exposure in Witwatersrand gold-miners without radiological silicosis. These authors also recorded that exercise capacity appeared best in those men whose dust dosage was highest. It is possible, as the present findings suggest, that including ex-miners may lead to an effect of dust on lung function being underestimated. On the other hand we were unable to improve the rather unconvincing effect of dust dosage on symptoms and I.M.B.C. in our Leigh survey (Table 16) by analysing miners and ex-miners separately. If dust were as important as is often thought one would have expected that the miners with simple pneumoconiosis, who have been exposed to a larger average dose of coal dust during their working lives, would have been more affected by bronchitis and disability than the miners without such radiological changes. Our findings suggest that there is little difference between them.

Short-term studies before and after the shift carried out at this unit have supported the observations of Pestiaux, Gielen, Degueldre, and Lavenne (1955) and Worth, Valentin, Gasthaus, Hoffman, and Venrath (1955) that there is no reduction in ventilatory capacity during the course of a single shift. Furthermore, preliminary observations on new entrants into mines in the Rhondda suggest that the ventilatory capacity is little affected by present dust levels though these are probably now much lower than they were in the past.

Other factors in mining might be responsible for the difference between miners and non-miners. Miners are for example engaged in heavy work, exposed to fumes underground during shot firing, and liable to changes of temperature during their day's work. We have no evidence to incriminate any of these factors, which are in any case not confined to mining. Possibly further light may be thrown on this subject by the National Coal Board's Field Research scheme and by follow-up studies of various population samples already studied, some of which are already being undertaken. At present it seems reasonable to conclude that while exposure to coal dust is one of the factors causing chronic non-specific respiratory disease it is unlikely to explain all the difference in this respect between miners and the rest of the community.

Cause of the Regional Difference.—While it is hard to explain the difference in chronic respiratory disease between miners and non-miners adequately it is even harder to explain the difference between miners in the Rhondda Fach and in Staveley. Briefly there are three possibilities. The difference could be due to variations either in the quantity or in the quality of the coal-mine dust in the two places; or, it might be due to differences in the amount of occupational selection occurring in them or, to differences in the amount of migration into and out of the areas. We have unfortunately insufficient information on any of these points to do more than speculate. Cochrane (1958) related the prevalence of simple pneumoconiosis in miners in Staveley to the length of time they had worked on the coal-face and concluded that the concentration of dust in Staveley mines was unlikely to have been greatly different from that in the Rhondda mines. Miners in Staveley tended to go on the coal-face some five years later than they did in the Rhondda and, consequently, had a somewhat shorter period of dust exposure. Cochrane however concluded that quantitative differences between the two areas could not explain the differences in ventilatory capacity. The possible importance of the age of entry into mining was considered by Worth *et al.* (1959). Their results suggested that differences in residual and functional residual volume between miners and non-mining controls were larger in those entering mining early in life. The early age at which the Rhondda miners started work on the coal-face might therefore be a contributory factor in the regional difference in respiratory disease.

There are certainly qualitative differences in the dust in the two areas, the coal of the Rhondda being of higher rank than that of Staveley. No evidence of differences in the morbid anatomy of miners' lungs in the two areas has yet been produced. Most comparisons have been concerned mainly with the more specific changes of pneumoconiosis and it might be useful to compare the lungs from the point of view of bronchitis and emphysema.

The hypothesis that emigration of the fitter members of the mining community from the Rhondda during the 1920's and 1930's has depleted the cohort of men who are now between the ages of 55 and 64 and has left us with a group with a lower lung function is considered in detail elsewhere (Cochrane and Higgins, 1961).

We should like to thank our colleagues at the Pneumoconiosis Research Unit; particularly Dr. J. C. Gilson, Director, for valuable advice and criticism; Mr. J. Thomas, for statistical assistance and the members of the field survey team who helped with the collection and analysis of the material.

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CARBON PNEUMOCONIOSIS

BY

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The occurrence of carbon pneumoconiosis in rubber-factory workers is unusual: the case reported here was discovered in a routine post-mortem examination. The report includes the clinical, radiological, morbid anatomical, and histological findings on a man who had worked in the carbon black store of a rubber works for a continuous period of 21 years, followed by 11 years in the calender department of the same factory. At the age of 65 years the man was retired on the grounds of age and indifferent health: he collapsed and died soon afterwards.

The medical history of severe cough with expectoration suggested that he may have had pulmonary tuberculosis in earlier life and some supporting evidence of this infection was found in that his wife contracted this disease after marriage and subsequently died from tuberculosis.

The appearances of massive fibrosis in the upper lobes of the lungs suggested that the combined action of carbon black and tuberculosis had produced an "infective" type of pneumoconiosis: in the lower lobes there was far less fibrosis and the appearances were those of simple pneumoconiosis. In addition to the fibrosis the lungs showed nodules of black dust with severe perifocal emphysema. Electron microscopy of the lung dust showed two distinct components and they were similar to samples of channel and thermal blacks which were the main types of carbon used in the factory.

This case is an example of pneumoconiosis due to virtually non-siliceous carbon and illustrates that prolonged exposure to heavy dust concentration produces such lesions as described in this paper.

Most of the published work on carbon pneumoconiosis is concerned with radiological appearances (Lochtkemper and Teleky, 1932). Gärtner and Brauss (1951) described lung changes in soot workers which were those of simple pneumoconiosis: in none of these cases was there evidence of massive fibrosis.

Koelsch (1952) described a condition of "pure carbon lung" which he found in electrode workers who had handled a pure form of carbon with very little silica contamination. He called it an advanced stage of carbon pneumoconiosis and not silicosis. Radiologically there were nodulation and conglomerate shadows with massive fibrosis. With so low a silicic acid content in the dust he was unable to explain the radiological findings, which were similar to soot workers' "silicosis" of the second and third degrees. In this paper, Hollmann is quoted as saying that carbon electrode workers are in danger of silicosis.

Meiklejohn (1957) studied the radiological changes in a group of carbon black workers and found the reticulation of simple pneumoconiosis: in a second group handling carbon with a small amount of mineral impurity, one man showed the radiological appearances of pneumoconiosis with fibrosis (category 2A) (International Labour Organization, 1953).

Vaccarrezza (1958) described lung changes in a man who had been shovelling charcoal for several years and Watson (in Gough, 1959) described changes in the lungs of a carbon electrode worker.

In all these papers, excepting that of Watson, the evidence is entirely radiological: histological examination could not be made as the workers were alive and had not undergone surgery to the lungs.

From the findings of these and other workers it appears that pneumoconiosis can be caused by carbon and other relatively inert dusts containing little or no siliceous material. Even if the small amount of silica present does cause fibrosis, the pathology is so different from that seen in pure silicosis that it is best not to use the word silicosis in describing it (Fletcher, 1952).

Amongst the forms of occupational lung disease carbon pneumoconiosis, other than in coal-miners, is fairly uncommon: in a rubber-factory worker it must be very unusual (Meiklejohn, 1956). The

following case which was discovered at a routine necropsy performed for H.M. Coroner, appears to be an example of "pure carbon" pneumoconiosis.

Case Report

Occupational History.—From the age of 17, until his retirement at the age of 65, A.W. worked almost continuously in rubber factories in one town: the only breaks were two years' military service in the 1914–1918 war and almost two years' unemployment soon after the war. In 1959 he retired and a few months later he died.

For a continuous period of 21 years (1927–1948) he worked in the carbon black store where the main ventilation was a doorway which opened on to a partially covered alley way.

The carbon, in 50 lb. bags, was stacked at the back of the store and from this pile the workman dragged the bags across the floor, opened them, and poured the carbon into tubs placed on a scale until the correct weight was obtained. Even with pelletized carbon this procedure creates thick clouds of dust; before pelletization the amount of carbon in the air must have been appalling.

When the correct amount of carbon has been weighed out, the tubs are wheeled across the alley and placed on a conveyer system which leads to the mixer: whilst on the conveyer various other fillers such as zinc oxide are added. In the mixing machine the fillers and molten rubber are mechanically blended.

During the 1939–1945 war years A.W. regularly worked in the carbon black store for up to 54 hours a week. During the whole of his time in this store he never wore a mask nor took any precautions to avoid contamination. The carbon black filled his clothes and soiled his skin to such an extent that he was strongly discouraged from sitting in a bus or train when travelling to and from his work. Attempts to remove the dust from his skin were relatively unsuccessful: he used various proprietary preparations and visited the local baths weekly, but with little improvement. He went occasionally to another town to have a Turkish bath and the results were more satisfactory.

He paid little heed to objections from his wife and others about his personal appearance. He enjoyed his work in the "blacking shop" because of the extra pay and relative independence: advice about contamination was disregarded. At night he slept in a separate room; his wife made him a special hood for his head and a long type of nightdress for his body in order to reduce soiling the bed clothes.

From 1948–1959 he worked as a sweeper in the calender department where rubber is coated on to a fabric base in the production of conveyor belting and similar items. The air in the calender section contained traces of carbon black and also talcum powder which was used to prevent the slabs of rubber adhering: there were also traces of sulphur, zinc, and magnesium oxides in this atmosphere but the amounts were very small. He never worked in the talc section.

Medical History.—A.W. had a persistent hard cough, with a small amount of black sputum for about 30 years and at times he was "short of breath" in the night. He married in 1928 and at that time his wife was healthy. Three years later she developed chest symptoms. In 1940 tuberculosis of the spine was diagnosed and treated. She died in 1942.

In 1949, when he had an attack of dermatitis, he was moved from the carbon store to the calender department and employed as a sweeper. In 1956 he began to notice mild exertional dyspnoea which slowly increased, and the cough with sputum became more marked.

A chest radiograph was taken in 1956 and again in 1958 when the mass miniature radiography unit visited the factory. These radiographs showed generalized reticular appearances throughout both lung fields with increased lung markings and fibrosis, especially in both upper zones.

Standard sized radiographs were taken and showed that in the left upper zone the fibrous mass was displaced downwards to the hilum by what appeared to be emphysematous bullae or pneumothorax, probably the former. The massive shadows were connected to the hilum and the apex by trabeculae and fibrous strands which are often seen in cases of tuberculosis and are due to thickened and fibrogenic bronchi. There was no evidence of active tubercle (Fig. 1).

Professor A. L. Cochrane reviewed the films and reported progressive, massive fibrosis of both upper zones.

He was examined by Dr. Geake (Consultant Chest Physician) in 1958. His general condition was good, his chest movement was poor and there was no added sound or localizing abnormal sign. The sputum was not examined bacteriologically. Dr. Geake considered that the radiological appearances were due to some form of pneumoconiosis and suggested the possibility of harmful dust to which the patient might have been exposed in the rubber factory.

Further examination of his past history revealed attacks of dizziness and fainting. On two occasions whilst on holiday, once in 1955 and again in 1958, he collapsed and was ill for a few weeks. His recovery was fairly rapid and he resumed his normal work in the factory. In 1959, whilst at work, he had another fainting attack and fell downstairs but did not sustain serious injury. After this the management suggested that he should retire.

After his retirement in February 1959 his cough became worse and he continued to expectorate a moderate amount of black sputum. His general condition was moderately good until about a week before his death (April 1959), when he seemed to lose interest in things and did not feel so well. He was found dead in his home, having collapsed whilst working in the kitchen.

Necropsy.—The only notable external feature was the generalized blackening of the skin. This was most marked on the palms of the hands and could not be washed off.

In the upper respiratory passages the mucosa was congested but not pigmented. Both lungs were enlarged, each weighing over 610 g.: they were intensely black

and large whitish emphysematous bullae were present at the apices and along the anterior margins. The upper lobes were severely contracted and fibrosed, the apical portions being largely replaced by enormous emphysematous bullae (Fig. 2). The posterior part of the upper lobes and the apices were firmly adherent to the chest wall and the interlobar fissures were closed by adhesions. The visceral pleura, covering most of the upper lobes, was thickened and, together with the remaining visceral pleura, showed peculiar speckled black and grey appearances with large, soft black velvety patches.

On palpation there were numerous, small, firm nodules scattered irregularly throughout the upper lobes; a smaller number were present in the lower lobes. There were no discrete palpable fibrous masses in any part of the lung substance.

On sectioning the lungs, the most striking feature was the copious oozing of black mucinous material from the cut ends of the bronchi and bronchioles: this secretion adhered to instruments, hands, and working surfaces. Two of the large emphysematous bullae at the left apex had penetrated the lung substance producing cavities measuring 7 × 3 cm. and 5 × 4 cm.; their walls were

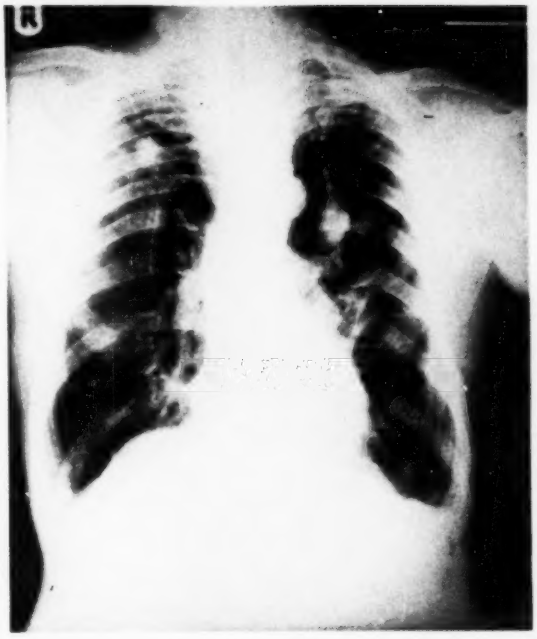

FIG. 1.—The chest radiograph shows complicated pneumoconiosis with massive fibrosis in the upper zones and emphysematous bullae at the apex.

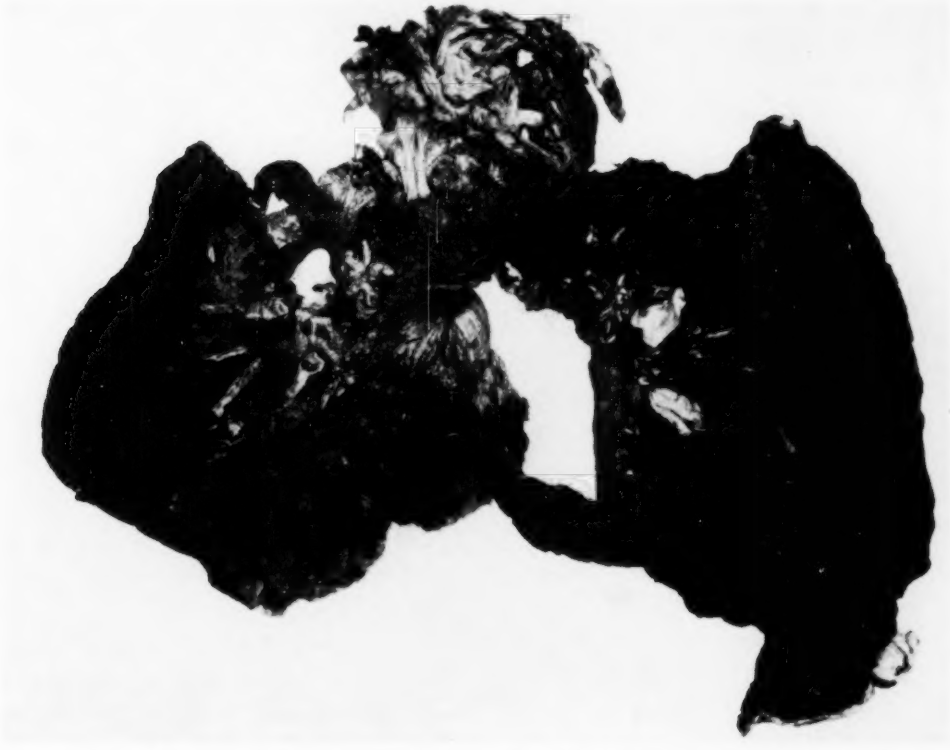

FIG. 2.—Formalin-fixed left lung. This photograph is a light print in order to show detail. The lungs were much darker than the print suggests: they showed severely scarred and contracted upper lobes with large apical emphysematous bullae.

FIG. 3.—A piece of stomach wall showing the mucosa speckled with deposits of carbon black (× 2).

black, ragged, and contained tendrils and strands of necrotic tissue. A smaller bulla at the right apex showed similar appearances. In the lower part of both upper lobes there was fibrosis with thick walled bronchi: enlarged pigmented lymph nodes were found at the hilum. In both lower lobes the cut surfaces were intensely black, the lung substance largely obscured by sticky black material: there were numerous small, poorly defined, black nodules (not exceeding 5 mm. in diameter) surrounded by focal emphysema. Some of the larger nodules showed a central cavity containing black sludge. There was also slight generalized emphysema.

The remarkable features were the intense blackness of the lungs, the white ballooned appearances of the apical bullae associated with cavitation of the upper lobes, marked fibrosis of the upper lobes, the small pneumoconiotic nodules distributed irregularly throughout the lung substance and the slightly generalized emphysematous character of the lungs. There was no evidence of tuberculosis.

It was subsequently noted that the intense blackness of the lungs remained unaltered after they had been immersed in several changes of formalin; the fixative was changed to inky black fluid with considerable tarry black sediment.

Other abnormalities which were probably related to the deceased's occupation were found in the lower end of the oesophagus and the cardiac end of the stomach (Fig. 3). The mucosa was speckled with spherical and irregularly outlined collections of black pigment measuring from about 2 to 6 mm. in diameter; there was one elliptical area measuring 15 × 5 mm. These pigmented patches were firmly adherent to the mucosa and resisted attempts to remove them by washing and rubbing. The pigment was similar to that found on the serous surfaces of the lungs.

The heart showed mitral stenosis due to healed rheumatic endocarditis: there was slight cor pulmonale: the main coronary arteries were partly occluded by atheroma. The kidneys showed granularity and arteriosclerotic changes. The brain showed marked internal hydrocephalus.

The cause of death was bacterial and rheumatic endocarditis and pneumoconiosis.

HISTOLOGY.

Lungs: The general features were those of collagenous fibrosis with small fibrous nodules; well-marked focal and slight general emphysema (Fig. 4). The mucosa of the bronchi and bronchioles showed partial atrophy of the epithelium and dense infiltration with black pigment: their lumen contained desquamated epithelium, clumps of black pigment, and dust-laden phagocytes. There were moderate amounts of inflammatory exudate but bronchopneumonia was not seen.

Typical reticulin fibrosis was seen around many of the bronchioles but the predominant appearance was linear and radial collagenous fibrosis with dense pigmentation (Fig. 5). In many areas the heavy dust infiltration completely obscured the collagenous tissue.

Around bronchioles and blood vessels there were pigmented nodules, singly and in clusters, which had caused marked collagenous reaction. In the upper parts of the lungs the nodules tended to coalesce to form larger nodules (Fig. 6). The smaller type of nodule measured up to 5 mm. in diameter and was surrounded by focal emphysema. The larger nodules, measuring 5–10 mm. in diameter, consisted of densely pigmented, whorled hyaline fibres showing some resemblance to silicotic nodules; some of these larger ones showed central liquefaction (Fig. 7), the cavity containing a sludge of pigment, leucocytes, and necrotic tissue; they were not the typical laminated type seen in classical silicosis but suggested the "infective nodules" of "complicated" pneumoconiosis described by Gough (1947); the appearances suggested progressive massive fibrosis.

The wall of the large emphysematous cavity in the left upper lobe showed linear and radial fibrosis, the tissue being obscured in parts by the dense pigmentation. Deeper parts of this region, which extended almost to the hilum, contained thick fibrous strands in which residual fragments of bronchial walls and blood vessels were seen.

Lymph nodes in the parabronchial tissue showed fibrosis with pigmented areas. In the lower lobes the appearances were mainly those of simple pneumoconiosis (Figs. 8, 9); there were areas of collagenous thickening of alveolar walls, many of which had become confluent

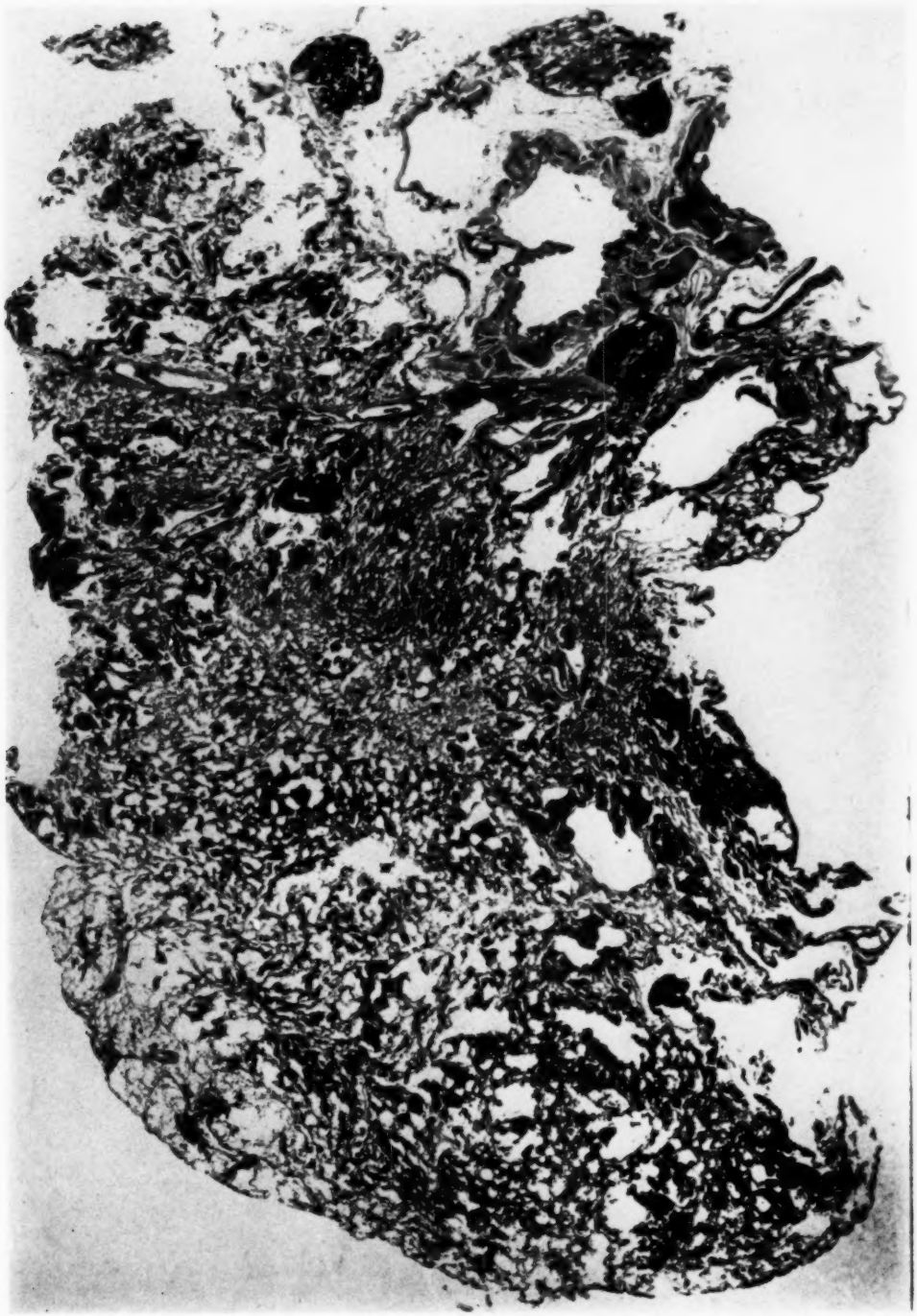

FIG. 4.—A large section of the left upper lobe in the perihilar region showing massive fibrosis characterized by densely pigmented thick collagenous strands and fibrous nodules: also widespread focal emphysema. Other areas show pigmented nodules, severe focal emphysema, and moderate fibrosis. (Van Gieson × 2·6.)

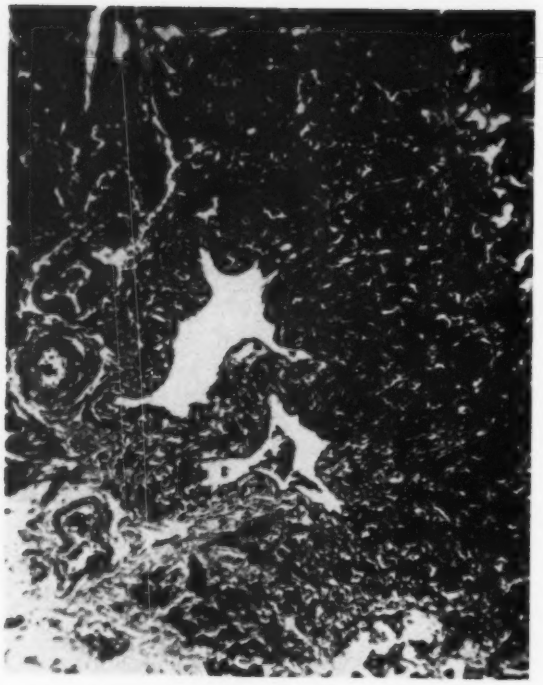

FIG. 5

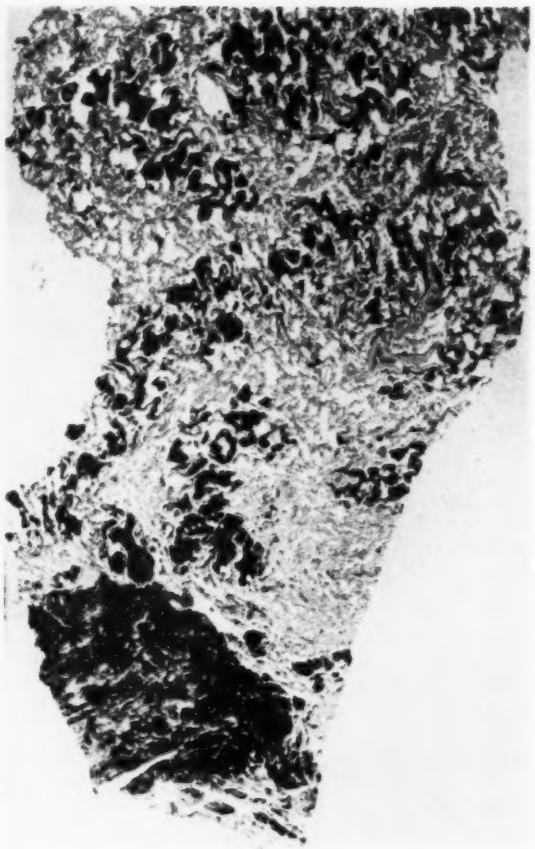

FIG. 6

FIG. 7

FIG. 5.—A lung field showing a dense mesh-work of coarse reticulin fibrils, surrounding blood vessels and bronchioles: also tangled pigment-laden collagen fibres. (Reticulin stain × 60.)

FIG. 6.—In this section there are single and groups of pigment aggregates showing a tendency to coalesce to form larger collagenous nodules: the large nodule shows little resemblance to the typical silicotic lesion. (Haematoxylin and eosin × 7.)

FIG. 7.—This illustrates a large liquefied nodule emptied of pigment sludge in the wall of a bronchus: also smaller nodules which show no softening. (Haematoxylin and eosin × 5.)

FIG. 8 (*opposite*).—A large area of the right lower lobe showing much less marked fibrosis and emphysema; the appearances resemble simple pneumoconiosis. (Haematoxylin and eosin × 3.28.)

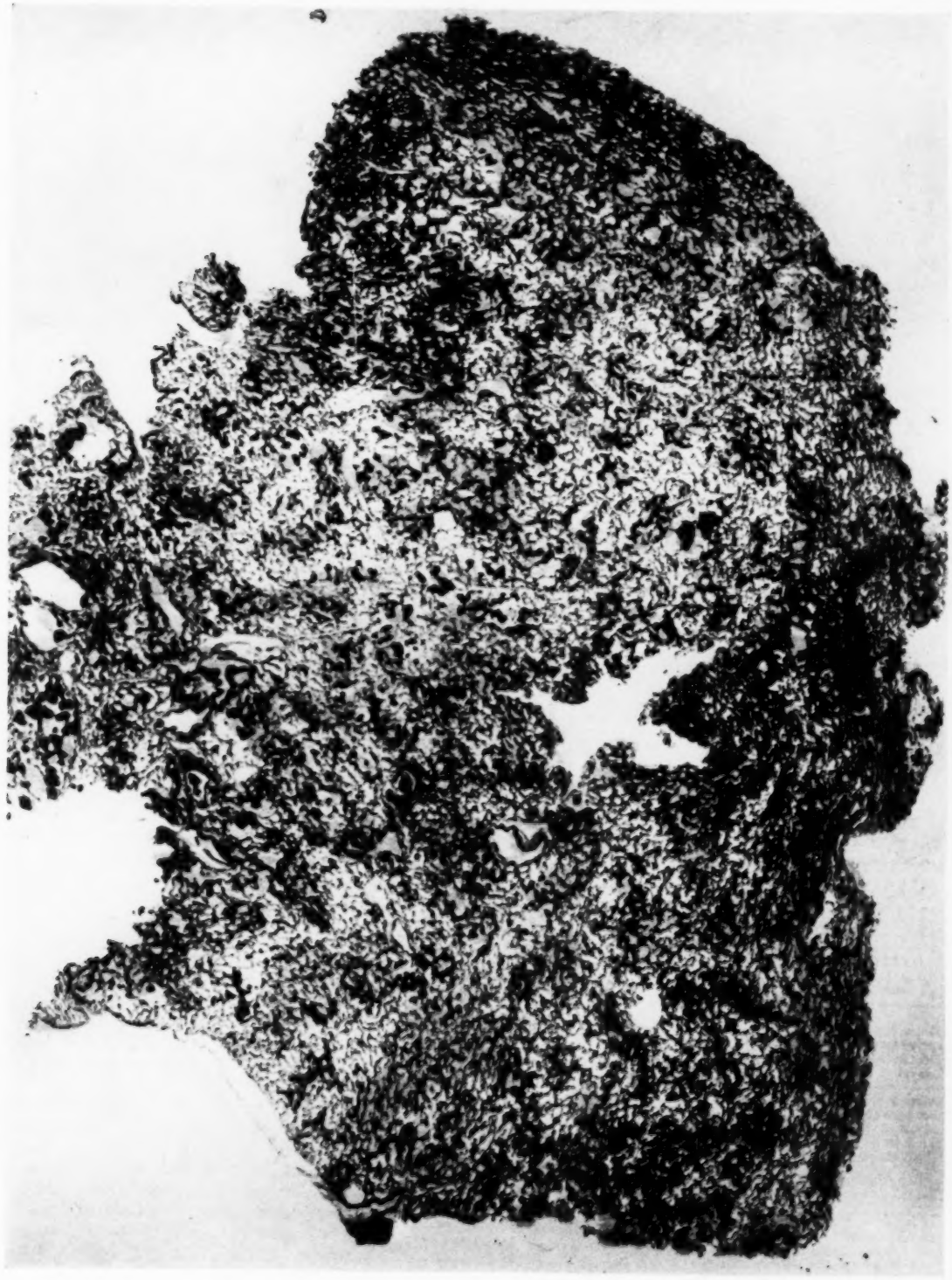

FIG. 9.—A field in the same lobe as Fig. 8, at a higher magnification showing very few pigment aggregates and only slight focal emphysema. (Lendrum's Melling Yellow × 63.)

TABLE I

DETERMINATIONS OF ASH AND QUALITATIVE SPECTROGRAPHIC ANALYSIS

	Case Reported Here (A.W.) (two samples)		Adult Male Town Dweller		Case of Pneumoconiosis in a Coal-miner
A: Ash (as % weight of dried formalin-fixed tissue)	1·164	1·313	0·865	0·990	3·147
B: Ash (as % weight of dried formalin-fixed tissue) after removal of NaCl	0·427	0·450	0·275	0·289	2·030
Qualitative spectrographic analysis of the ash in B					
Fe	±	+	±	+	+
Si	±	±	±	±	+ + +
Al	—	±	—	—	+
Mg	—	±	—	—	+

+ + + Present in large amounts.
+ Present in small amounts.
± Present in trace amounts.
± Present in slight trace amounts.

forming bands of dust impregnated collagenous tissue. Inside the alveoli there were numerous pigmented phagocytes similar to those seen in the bronchioles.

Vascular changes were conspicuous. Most of the smaller and many of the larger arteries showed thickened intima, in some instances the lumen was occluded by recanalized fibrous tissue. Portions of the internal elastic laminae along with neighbouring media and adventitia were necrotic and had been replaced by collagenous tissue densely infiltrated with black pigment; the appearances were similar to those described by Geever (1947).

When examined by polarized light numerous sections and samples of the lung dust showed no optical activity. Incinerated sections showed that most of the pigment was combustible and optical activity was not seen after heat and acid treatment. Some iron which was present in the incinerated sections was thought to be of haematogenous origin. An exhaustive search for asbestos bodies and the "curious bodies" found in talc pneumoconiosis (McLaughlin, Rogers, and Dunham, 1949) gave negative results. A large number of sections and numerous films made from the material in the liquefied nodules were examined for tuberculosis and also gave negative results.

Stomach: Small areas of gastric mucosa and submucosa were infiltrated with deposits of carbon black; many of the mucous glands which were peppered with the black dust appeared atrophied. The carbon had presumably been swallowed along with sputum.

Skin: Naked eye appearances suggested that the pigment had penetrated to the dermis but this was not confirmed by microscopical examination.

Carbon deposit was not found elsewhere in the body.

Physico-chemical Examination of Lungs and Lung Dust

A preliminary chemical examination of portions from the lungs of the deceased was made by Mr. A. Thompson and the results compared with a normal control and samples from a coal-miner with pneumoconiosis (Table 1). The samples of lung were dried at 105° C. and then ashed (line A.). As the lungs had been fixed in formol-saline the salt was removed and the ash, as a percentage of the dried tissue, recalculated (line B). The ash, after removal of sodium chloride, was examined spectroscopically and gave the qualitative results shown.

This rough analysis suggested that the chemical composition varied throughout the lung and that the lesion was chemically markedly different from the pneumoconiosis found in coal-miners when siliceous rock had been encountered.

The deposit which was washed from the lungs during histological fixation was purified and examined by electron microscopy (National College of Rubber Technology) with the following results:

"The specimen shows the presence of spherical particles which form agglomerates and chains giving an appearance typical of the behaviour of carbon black. The approximate particle diameter of 0·1 microns being of the order found in fine thermal black."

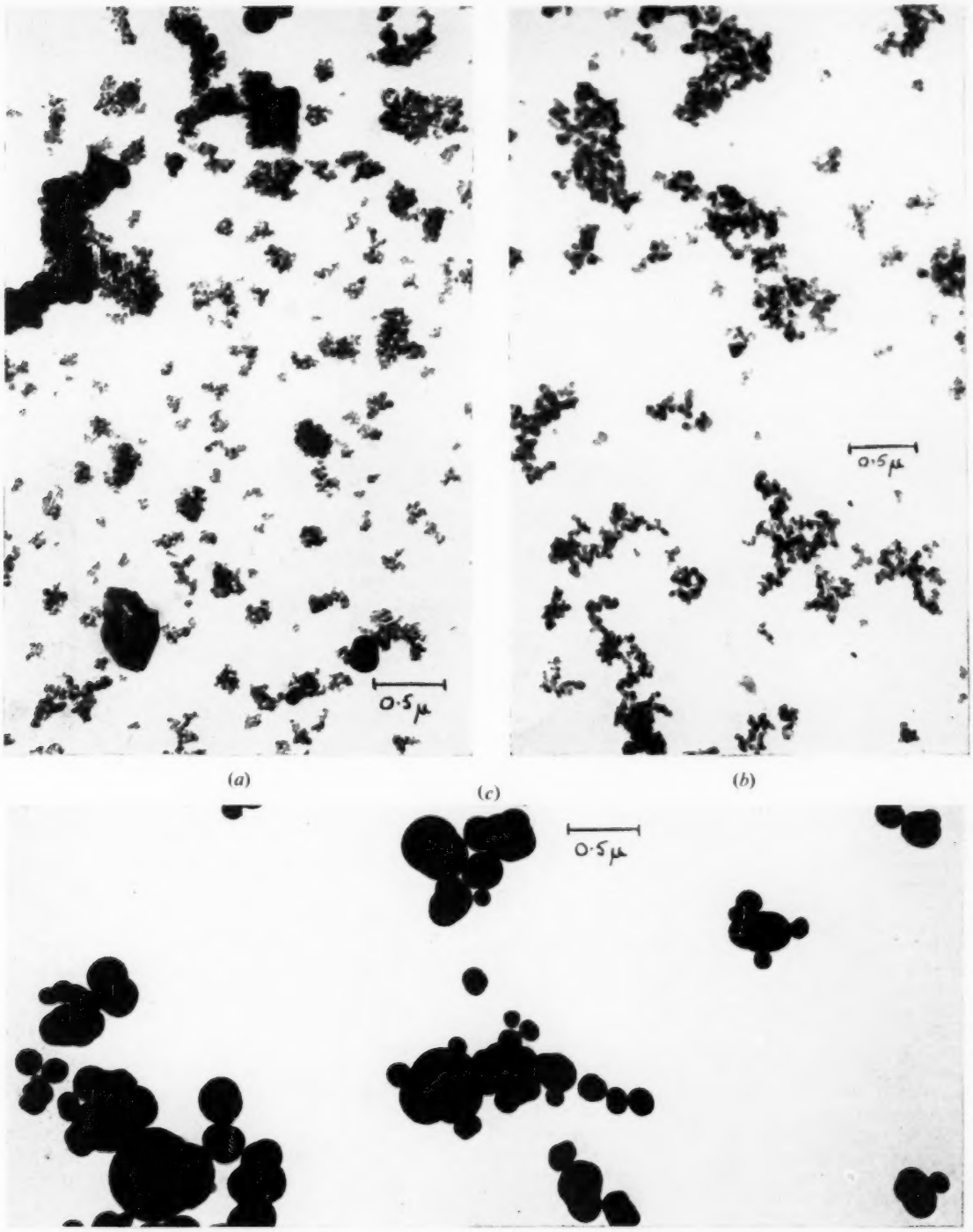

FIG. 10.—(*a*) Electron micrographs of lung dust × 21,000. There are two components, very fine and coarser particles which are similar to the forms of carbon black with which A.W. had worked. The very fine particles are similar to furnace black (*b*) and the coarser particles to thermal black (*c*).

FIG. 9.—A field in the same lobe as Fig. 8, at a higher magnification showing very few pigment aggregates and only slight focal emphysema. (Lendrum's Melling Yellow × 63.)

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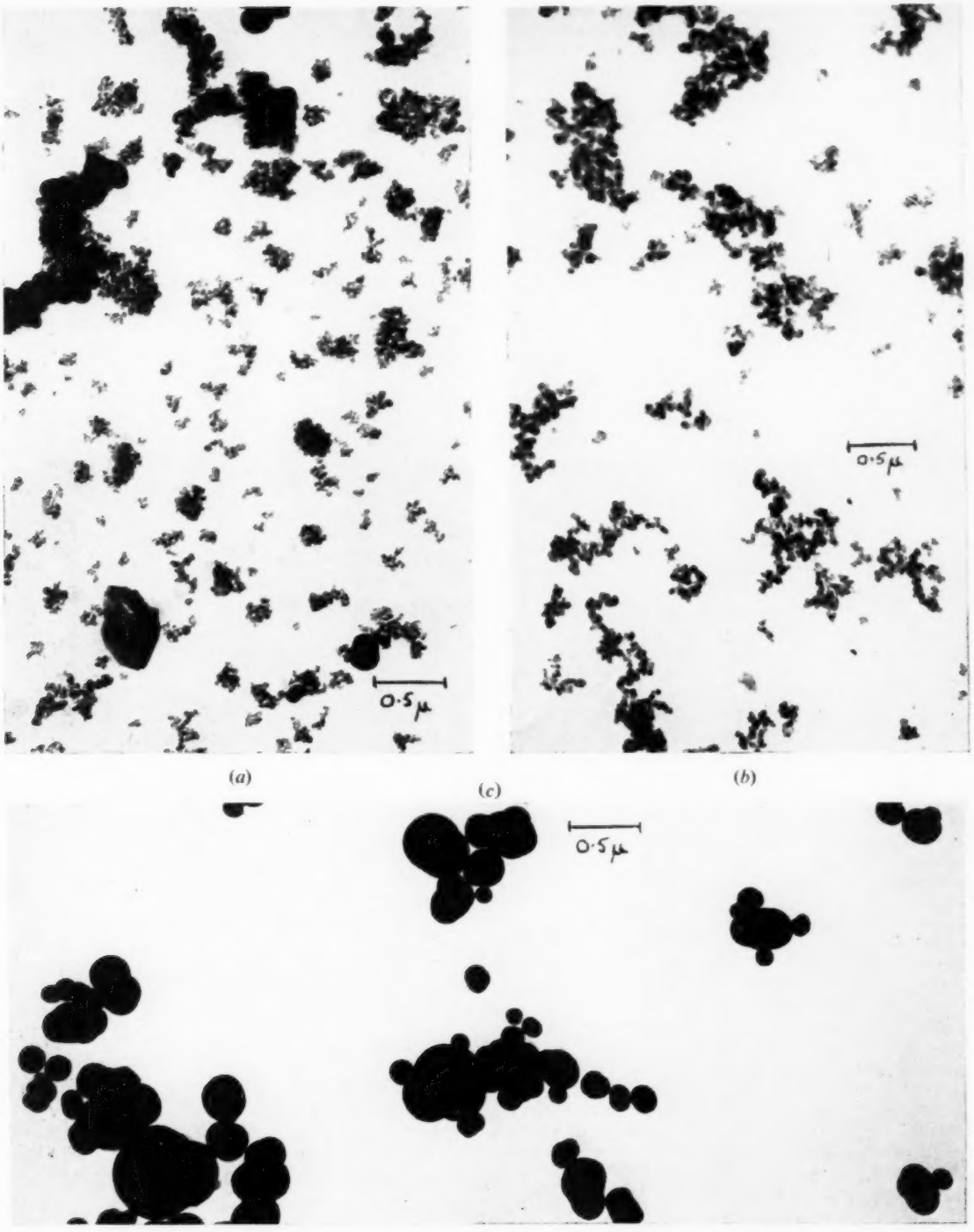

FIG. 10.—(*a*) Electron micrographs of lung dust × 21,000. There are two components, very fine and coarser particles which are similar to the forms of carbon black with which A.W. had worked. The very fine particles are similar to furnace black (*b*) and the coarser particles to thermal black (*c*).

As these preliminary examinations had proved interesting, it was thought that a more detailed examination should be made and this was undertaken by Dr. Nagelschmidt of the Safety in Mines Research Establishment in Sheffield.

Samples from various parts of the lungs were dried, ground, and treated with concentrated hydrogen peroxide to isolate the dust. The dust amounted to 15% of the dried lungs: 90% of the dust was carbon and 10% ash. The ash, which had been obtained at 450° C., contained 27% SiO_2 and 10% Fe_2O_3: its ignition loss at 850° C. was 7·5%.

X-ray diffraction analysis of the ash showed a little mullite and talc with doubtful traces of quartz and cristobalite.

Electron microscopy showed two main components (Fig. 10a). The finer particles (20/30 mμ in diameter) were similar to furnace and channel blacks: the coarser particles (200/400 mμ) were similar to thermal black. The samples used for comparison were of the types with which he had worked (Figs. 10 b, c).

Carbon Black.—Carbon black, in the sense in which we use it, includes all forms of carbon prepared by the channel, furnace, lampblack, and thermal processes: these carbons are chemically distinct from bone-black, charcoal, and chimney soot. Graphite differs in that it is crystalline and, in the natural state as mined, contains up to 25% of siliceous material by weight.

Chemically, carbon blacks are essentially carbon combined with hydrogen and oxygen. The hydrogen derives from the hydrocarbon used in manufacture and is thought to be attached to the carbon atoms by true valency bonds giving an unsaturated condition. The chemisorbed oxygen affects the hydrophilic properties of the black and these properties are of importance to the rubber industry. There are various other contaminants in carbon used commercially; these depend on the hydrocarbon source and the method of manufacture: they include various volatile benzene-soluble substances, iron oxides from the channels or pipes and calcium salts from the quenching water used in manufacture. The ash content is usually less than 0·1% but some furnace blacks may have up to 1% ash, which is mainly iron oxides. Silica oxides are present in very small amounts or not at all. Samples of channel and furnace blacks, which we checked, gave ash values of 0·038 and 0·047%: the ash contained iron and calcium compounds; silica was not detected.

The rubber works concerned in this case uses large amounts of furnace and channel blacks with very small amounts of lamp and acetylene blacks. The carbon is used as a reinforcing filler, its main effect being to increase stiffness, modify tensile and tear strengths, and increase abrasion resistance. Stiffness is proportional to the absolute amount of filler added: tensile strength increases as particle size decreases, abrasion resistance is generally dependent on particle size but different methods of carbon manufacture have some effect. The particle size of the carbon used in the rubber industry is generally in the range of 20 to 500 mμ. Owing to the small particle size required in rubber manufacture it is obvious that fine carbon dust will always be a problem in rubber works.

Discussion

This case raises matters of considerable importance in the aetiology of pneumoconiosis. The radiological and pathological findings were those of progressive massive fibrosis and resembled the advanced stage of coal-workers' pneumoconiosis with dense collagenous fibrosis and "infective nodules" in the upper parts of the lungs. The man had been exposed to carbon black for the greater part of his working life: 21 years were spent in the carbon black store where the dust concentration was very high. There had been no occupational risk in any other employment. The most likely explanation of the massive pulmonary fibrosis appears to be the combined action of carbon black and tuberculosis. Pulmonary tuberculosis in youth or middle age cannot be excluded owing to inadequate information and lack of bacteriological investigation. In fact, the history of a persistent cough, with sputum for many years, together with the presence of spinal and probably pulmonary tuberculosis in his wife some years after they were married, strongly suggests that he may have been infected.

In 1956 and 1958, when the patient was well over 60, the clinical and radiological examinations of his chest were negative for active tuberculosis, the probable infection having died out. At necropsy, when the deceased was aged 65, the usual microscopical and animal tests for tubercle were not done because the clinical data were not available. In the histological preparations of the lung tissues and in the sludge from the liquefied nodules *Tubercle bacilli* could not be demonstrated microscopically.

Another interesting feature in this case is the development of pneumoconiosis in the virtual absence of quartz: this is not entirely new. In his radiological examinations of carbon electrode workers, Koelsch (1952) suggested that carbon alone could cause proliferative changes in lungs and that carbon deposits could produce local circulatory disturbance and thus give rise to induration. The carbon or anthracite which they handled contained less than 1% of ash, including small amounts (0·001 to 0·003%) of silica, mostly in the form of silicate. He found advanced stages of pneumoconiosis with nodulation and conglomerate shadows. There was no pathological examination in any of his cases.

More recently, Watson (quoted by Gough, 1959) investigated the case of a man making carbon electrodes who was exposed to the dust of anthracite

and coke. The changes in his lungs were indistinguishable from the massive fibrosis of coal-miners, yet these lungs, on careful analysis by Nagelschmidt, revealed very little quartz. *Tubercle bacilli* were grown from the lungs although the usual histological evidence of tuberculosis was lacking. There was simply the necrosis, which one often sees in coal-miners' lungs, which is due to the action of *Tubercle bacilli* but is unaccompanied by the usual endothelial and giant cell reaction.

During the chemical analysis it was noted that the burning characteristics of the carbon recovered from the lungs were different from those exhibited by the carbon to which the man was exposed. This was probably due to alteration of the hydrogen, oxygen, and volatile components by the physiological processes of the lungs.

It was also noted that areas of lung tissue, mainly in the lower lobes, suggested the appearances of simple pneumoconiosis without the additional effect of probable tuberculosis: there were few nodules, less marked emphysema, and minimal fibrogenic effect. That a relatively inert dust, such as carbon black, which contains very little free silica, can produce simple pneumoconiosis is now well recognized (Fletcher, 1952) and appears to bear some relation to pneumoconiosis due to inhalation of soot. The main differences between carbon black and soot are the smaller particle size of the former and the lesser surface adsorbed contamination with volatile organic matter. In cases of soot pneumoconiosis Gärtner and Brauss (1951) found that heavy exposure to soot inhalation could continue for many years before pneumoconiotic effects were seen on radiological examination. There is no pathology in any of the cases reported.

In the case under consideration prolonged exposure to heavy clouds of carbon was required to produce this degree of pneumoconiosis. It is also noteworthy that none of the other workers in the same factory, one of whom was employed in the carbon black store for 11 years, has developed pneumoconiosis. The study of this case suggests that carbon pneumoconiosis, whether simple or "infective", requires prolonged exposure to a heavy concentration of inert dust unless the workman happens to be allergic to the carbon or the organic contaminants which it bears.

We are indebted to H.M. Coroner for permission to publish this case: to Professor J. Gough for reviewing the histological findings and referring us to the literature: to Professor A. L. Cochrane for his opinion on the chest radiographs: to Dr. A. Meiklejohn for helpful advice: to Dr. A. T. Doig for most helpful reviews of the pathological and radiological appearances: to Mr. A. Thompson of the N.W. Forensic Science Laboratory, Preston, for chemical analysis: to Dr. G. Nagelschmidt of the Safety in Mines Research Establishment, Sheffield, for chemical and *x*-ray diffraction analysis and, together with the National College of Rubber Technology, for electron microscopy: to Dr. M. R. Geake for access to radiographs and medical history: to Messrs. J. H. Wilkinson and J. Urquhart for technical assistance.

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CARBON PNEUMOCONIOSIS IN A SYNTHETIC GRAPHITE WORKER

BY

W. B. LISTER

From the Pneumoconiosis Medical Panel, Manchester

(RECEIVED FOR PUBLICATION AUGUST 31, 1960)

A case of carbon pneumoconiosis is described and discussed. A man, aged 60, who had been turning and grinding synthetic graphite bars for 17 years, developed pneumoconiosis, Category 3. In conjunction with others previously published, this case confirms that pneumoconiosis can be caused by " nearly pure " carbon of low ash content and a wide range of particle size after long exposure to synthetic graphite or carbon black dust.

Miller and Ramsden (1961) described a case of carbon pneumoconiosis mainly from the pathologist's point of view and included a description of the chemistry of carbon black, and reference to these two aspects is therefore omitted.

A considerable literature on carbon pneumoconiosis has accumulated in the past 30 years but closer scrutiny reveals only very few cases in which the dust was pure carbon or " nearly pure " carbon (Hollmann, 1928; Töppner, 1952; Rüttner, Bovet, and Aufdermaur, 1952; Meiklejohn, 1957). The conclusions drawn from these cases are oddly contradictory. Koelsch (1958) finds the evidence that lung fibrosis can develop without silica unconvincing. He thinks that pneumoconiosis, caused by pure graphite without any admixture of silica or silicates, may possibly be produced experimentally but hardly occurs in practice. Meiklejohn (1957) on the other hand says " it emerges that pneumoconiosis of the coalworkers' type, simple and complicated, can be caused in workmen by dust in which silica constitutes only a trace ". Similarly, Gough and Heppleston (1960) find " it may be concluded that free silica is not necessary for the development of the pure dust lesion in coalworkers . . . ".

In view of this divergency of views and the paucity of such cases the report of another example may be useful.

Case Report

In September 1959 the Manchester Pneumoconiosis Panel of the Ministry of Pensions and National Insurance saw a man aged 60. He had been a hod carrier in the building trade for 25 years, spent three years in the Forces, and since 1942 worked as a centre lathe operator in a small factory, turning and grinding bars of synthetic graphite. The bars are used in the manufacture of moulds for the forming of hard metals in electric furnaces.

There was nothing of note in the family history and he had had no serious previous illnesses. His first radiograph, taken by a mass radiography unit in 1953, showed diminished translucency on the left side and a hard nodule in the left apex. He continued at his job and chest symptoms started about two years later. He developed a cough with greenish sputum, pain in the midsternal region, dyspnoea on hills, tiredness and giddiness on exertion. He was referred to the Chest Clinic in November 1958 and the report mentions kypho-scoliosis, a fixed chest, and poor respiratory excursions. The radiograph showed coarse nodulation in both lungs. Another film in June 1959 showed no change. Sputum was negative for tuberculosis in the smear and culture. He made a claim for disablement benefit and was seen by the Pneumoconiosis Board three months later.

He was found to be of moderate physique, weight 10 stone, height 5 ft. 7 in., chest measurement 35 in./ 36½ in. There were no abnormal physical signs in his chest, his blood pressure was 170/90 mm. Hg, and indirect M.B.C. 73 litres/min. The chest radiograph showed pneumoconiosis, Category 3m (Fig. 1). Fig. 2, an enlargement of the left upper zone, shows the well-marked nodulation. A pulmonary function test (Table 1) was carried out later by Dr. C. Ogilvie at the Liverpool Thoracic Surgery Centre.

There was a moderate impairment of maximum breathing capacity and flow rates, a slight reduction in vital capacity, and a diffusing capacity at the lower limit of the normal range. Dr. Ogilvie considered the findings compatible with chronic bronchitis, probably with only a mild degree of either emphysema or fibrosis.

The dust exposure was 17 years and the material used was synthetic graphite made from carbonization

FIG. 1

FIG. 1.—Chest radiograph showing pneumoconiosis, Category 3m.

FIG. 2.—Enlarged radiograph of left upper zone showing nodulation.

FIG. 2

of oil or, as stated by the manufacturers, from petroleum coke which is wholly calcined and free from volatile materials. A dust sample obtained from the deposit on the work bench was examined by the Government Chemist and contained, by chemical extraction, less than 0·02% by weight of free silica. None was detected by *x*-ray method. Carbon accounted for over 90% by weight, with 0·45% ash and volatile matter and a trace of moisture. Spectrographic examination showed only traces of iron, silicon, magnesium, nickel, and calcium. Table 2 shows that the particle size ranged from below 0·6 μ to over 100 μ, the median size being 8·5 μ. The particle shape was irregular.

As the man had been grinding synthetic graphite bars on carborundum wheels there may have been some risk from the bonding material of the wheel as discussed by Posner (1960). However, as the dust sample contained only a trace of free silica, this can hardly be held

TABLE 2
RANGE OF PARTICLE SIZE

Maximum Size (μ)	Per cent in Size Range	Per cent up to Given Size
< 0·6	5·25	5·25
0·6	4·20	9·45
1·2	7·35	16·80
2·4	6·30	23·10
3·6	6·30	29·40
4·8	3·15	32·55
6·0	4·20	36·75
7·5	6·30	43·05
9·0	9·45	52·50
12·0	10·50	63·00
15·0	10·50	73·50
24·0	10·50	84·00
32·0	6·30	90·30
40·0	4·20	94·50
50·0	—	94·50
60·0	1·05	95·55
80·0	2·10	97·65
100·0	1·05	98·70
> 100·0	1·30	100·00

TABLE 1
PULMONARY FUNCTION TEST

	Lung Volumes (litres)	Mechanical Function	Before Adrenalin (litres/min.)	After Adrenalin (litres/min.)
Vital capacity	3·05	Maximum breathing capacity	46	48
Inspiratory capacity	1·71	F.E.V. 1 second	1·20 litres	1·32 litres
Expiratory reserve volume	1·35	Timed vital capacity	52%	52%
Functional residual capacity	2·83	Maximum inspiratory flow rate	150	133
Residual volume	1·48	Maximum expiratory flow rate	75	90
R.V./T.L.C. ratio	33%			

Diffusing capacity for carbon monoxide 18·6 ml./mm.Hg/min. (71% normal).

responsible for the radiological changes. There were four other men employed in the same room for more than five years but none at the same job. Two of them had chest radiographs taken in which we found nothing abnormal.

Discussion

It is interesting to compare some features of this case with those described in the literature. Unfortunately, the data in the few cases known are incomplete; for example, it is generally not stated whether the dust samples were collected from airborne or deposited dust. As regards particle size therefore, the figures are not very helpful but Rüttner's was 3 μ to over 30 μ, Meiklejohn's mainly less than 2 μ, and Miller and Ramsden (1961) found it generally less than 0·5 μ, compared with our median figure of 8·5 μ. As for ash content, the synthetic graphite in Rüttner's case contained 0·085%, and Meiklejohn mentions three different types of carbon, *i.e.* " nearly pure carbon " containing 0·01%, " retort carbon " 1·9%, and oven coke 0·5%. Miller's carbon black contained 0·038% and 0·047%, ours 0·45%. Length of exposure was 10 years in Töppner's case, 21 years in Rüttner's, 12 and 22 years in Meiklejohn's, 21 years in Miller's and 17 years in ours. The occupations concerned have been carbon stick workers (Hollmann), synthetic graphite mill worker (Rüttner), carbon black factory worker (Töppner), mixing and grinding lamp black with other grades of carbon produced from gas and oil cokes (Meiklejohn), mixing carbon black in rubber (Miller), and turning and grinding synthetic graphite bars in the case now reported. Progressive massive fibrosis is described only in one case by Hollmann, one by Rüttner, one by Meiklejohn, and in Miller's case. The symptoms are generally slight. There is occasional dyspnoea, cough, and sputum; also, in our case, midsternal pain, lassitude, and giddiness on exertion.

It is perhaps premature to draw any definite conclusions from the small number of published cases but it is to be expected that more will be detected with increasing awareness of the risk. The facts appear to be that pneumoconiosis, simple and complicated, can be caused by " nearly pure " carbon of any particle size from less than 0·5 μ upwards, with only traces of silica or silicates, an ash content of 0·01% to 1·9%, and an exposure of 10 to 22 years to synthetic graphite or carbon black dust.

I am grateful to the Chief Medical Officer, Ministry of Pensions and National Insurance, for permission to publish this paper, to Drs. J. C. McVittie and G. B. Murray of the Pneumoconiosis Panel for their help and encouragement, to Dr. W. Lee, Consultant Chest Physician, Salford, for clinical details and radiographs, to Dr. C. Ogilvie of the Liverpool Thoracic Surgery Centre, for carrying out the lung function test, to Dr. A. A. Miller, of Preston, for a preview of his paper, and to Dr. J. B. L. Tombleson, H.M. Medical Inspector of Factories, for liaison with the firm concerned.

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BYSSINOSIS AMONG COTTON WORKERS IN BELGIUM

BY

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The existence of byssinosis among cotton workers in Belgium has, up to now, been a matter of doubt. This study reveals that the disease undoubtedly occurs, but its prevalence is much lower than in Lancashire cotton mills. I have made investigations in two textile mills, one in East Flanders and one in West Flanders. Ninety-eight workers were interviewed in the first mill and 101 in the second, comprising card-room workers, thrashers, and blenders. Ten (5%) of these workers were found to have Grade I byssinosis; four (2%) were diagnosed as Grade II; and two (1%) were in Grade III.

Byssinosis is a respiratory disease affecting textile workers in the card-rooms of cotton-spinning mills.

The first physician in Flanders who drew attention to the specific influence of cotton dust was Van Coetsem who, in 1836, stressed the typical discomfort due to what he called " cotton pneumonia " at the beginning of the week.

In 1845, Mareska and Heyman found that among 1,000 men working in the cotton mills of Ghent, 49 were suffering from respiratory diseases. An inquiry among 1,000 female workers showed that 58 were similarly affected. All the workers declared that dust made them feel more uncomfortable at the beginning than at the end of the week. They described the uneasiness they felt as a " pack " weighing on their chest.

Nearly a century elapsed before Thiry (1941) surveyed 400 cotton operatives. Among the younger workers nothing abnormal was recorded, but 88% of the older workers had symptoms of chest diseases identified as chronic bronchitis or emphysema. But Thiry made no mention of the characteristic " Monday complaints ".

Present Inquiry

In 1957, the prevalence of byssinosis was investigated in two factories located in each of the well-known textile centres of Courtrai and Ghent.

These two factories were typical of Belgian textile mills. They were technically well equipped, without being very modern. Each employed roughly 1,000 persons of whom about 100 worked in the card-room and other processes in which cotton is prepared for spinning.

Card-room workers, thrashers, and blenders were interviewed and asked previously prepared questions about their family and occupational histories. Particular attention was paid to the number of years worked in cotton card-rooms and other processes in which cotton is prepared for spinning.

According to Schilling (1956), byssinosis should be diagnosed on the patient's symptoms of chest tightness and breathlessness. Belgian and other foreign specialists supported this view and advised me to rely on the patient's history for diagnosis. The histories were graded as follows:

Grade I: Subjective symptoms such as a suffocating feeling in the chest, limited to Mondays.

Grade II: Similar symptoms extending to other working days.

Grade III: Continuous symptoms during weekends and holidays.

Most of those who gave a history of byssinosis were sent to Dr. Op de Coul in Holland. He confirmed the diagnosis in all the cases seen. Some typical histories are given in the Appendix.

Results

The prevalence of byssinosis was similar in the two mills (Table 1).

There are three possible reasons why none of the women had symptoms. First, they operate machines which are believed to give off the smallest quantity of dust; second, they are less tied to their

TABLE 1

PREVALENCE OF BYSSINOSIS IN CARD-ROOM WORKERS, THRASHERS, AND BLENDERS

Mill	No. at Risk	Byssinosis Grade		
		I	II	III
A (Courtrai)	98	4	2	1
B (Ghent)	101	6	2	1
Total	199*	10	4	2

* Includes 32 women in Mill B and 39 in Mill A. No woman gave a history of byssinosis.

jobs than the men and can leave as soon as symptoms appear, and third, they smoke much less than the men.

Age.—Table 2 gives the distribution of prevalence by ages.

All six workers who had reached Grade II or III byssinosis were aged 41 years or more.

Years of Service.—No worker with less than five years' service in card-rooms was apparently affected by the dust. Among the 83 men who had less than 21 years' exposure, seven (8%) had symptoms but among those with 21 or more years' exposure, nine out of 34 were affected, giving a rather alarming prevalence of 26%.

Type of Work.—To know the kind of work done by the byssinosis patients helps us to find out which machines are the most dangerous.

The carding machines emit the greatest quantity of dust, but it would be unwise to neglect the operations before carding. The operations which follow the carding process are apparently without risk.

TABLE 2

PREVALENCE OF BYSSINOSIS BY AGE AMONG MEN

Age	No. at Risk	No. with Byssinosis
14–	4	0
21–	54	5
31–	21	0
41–	28	7
51–	16	3
61–65	5	1
Total	128	16

In this study, the following three operations gave rise to the disease:

Among the 21 workers occupied in blending (mixing room): one case;

Among the 22 workers occupied in thrashing (blowing room): two cases;

Among the 85 workers employed on the carding processes: 13 cases.

Thus, carding was responsible for most cases of byssinosis and confirms the general opinion among those acquainted with working conditions in cotton mills.

Attention has been drawn above to the possible reasons why female workers were not affected. The type of work may also be important. The women are not working on carding machines, but on other machines in other parts of the card-room. In Lancashire mills it has been shown that there is less dust and less disease in these parts of the card-room (Roach and Schilling, 1960). True, these machines form no part of the spinning mills and, though they are to be found in the same card-room, the quantity of dust is less.

For 20 years, byssinosis has been officially recognized as an occupational disease in Great Britain where, in the three years 1956–1958, 686 new cases out of some 40,000 workers at risk were awarded disability pensions (Gilson, 1960). As far as is known, byssinosis is not a compensatory occupational disease in any other country. This paper reveals that the disease undoubtedly occurs in Belgian cotton mills but the prevalence in the two mills studied is much lower than that found in Lancashire mills where as many as 56% of card-room workers may be affected (Schilling, 1956). It is hoped that in Belgium it will be possible to make a wider and more detailed survey of cotton mills to reach more definite conclusions about the size of the problem.

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APPENDIX

Examples of case histories of byssinosis are given below. They follow a similar pattern to those described by workers in other countries.

Grade I.—E.G., after nine years' work at a tile factory, became a carding machine operator 11 years ago.

Four years ago he developed so-called "Monday complaints" after two hours' work in the card-room. After leaving work in the evening he had to recover his breath, which took him about 20 minutes. At his former work he always felt well and now he sometimes had to gasp for breath. As he was worried about these symptoms

he went to a chest physician, who could find no abnormality.

Grade II.—V.D.B.A. aged 28, has worked in the card-room for 12 years. He has suffered from a skin complaint on forearms, knees, and thighs since he worked in cotton mills.

After six years, he had symptoms which he described as a " belt around his chest "; this feeling of discomfort, which at first occurred only on Mondays, spread later on to Tuesdays and Wednesdays and decreased in the second half of the week.

He smokes about 40 cigarettes daily. When he is away from work for about eight days, his chest symptoms and skin eruption disappear.

Grade III.—S.M. aged 53, started work at the age of 16 in the blending room and was appointed a card machine operator after three years of service.

Six years later he first noticed chest symptoms especially on Mondays when he complained of an oppressive feeling that gradually became worse and finally was experienced on other days of the week. At present, he has constant discomfort. His breathing difficulties cause insomnia and he has been forced to stop smoking.

His general practitioner at first thought him to be suffering from tuberculosis. A full investigation was negative and it was concluded that his disease was due to his employment on dusty work.

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THE ROLE OF BACTERIAL ENDOTOXINS IN OCCUPATIONAL DISEASES CAUSED BY INHALING VEGETABLE DUSTS

BY

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A large group of occupational diseases connected with the inhalation of various vegetable dusts, especially in the textile industry, have certain main symptoms in common such as fever, coughing, dyspnoea, and general malaise. In most cases the symptoms are more prominent on Mondays or on resuming work after one or more days of interruption. The symptomatology of these diseases and the Monday effect leads to the hypothesis that they are due to the inhalation of the endotoxins of gram-negative bacteria that contaminate the various vegetable materials, the Monday effect being connected with the phenomenon of tolerance to the endotoxins. Support for this view came from the demonstration of the constant presence of endotoxins in cotton dusts in textile mills and from the study of the effects of the inhalation of purified endotoxins in rabbits and man.

The pathological processes observed in workers exposed to the inhalation of different vegetable dusts are numerous and varied. Some of the diseases produced by these dusts have features in common such as attacks of fever, accompanied by respiratory disturbances, and the characteristic appearance or enhancement of symptoms on resuming work after one or more days of interruption, as on Mondays. These resemble some effects of the endotoxins of gram-negative bacteria, that are powerful pyrogens and are able to induce a local inflammatory response in the tissues; also the Monday effect might be compared to the ready loss of tolerance to endotoxins that follows discontinuation of exposure to these agents.

A reappraisal of the possible role of the endotoxins of gram-negative bacteria in the pathogenesis of occupational diseases caused by the inhalation of vegetable dusts, might be rewarding.

Presence of Endotoxins in Industrial Cotton Samples

One of the vegetable dusts most often recognized as responsible for occupational diseases is cotton dust. It was decided therefore to find out whether endotoxins were present in cotton samples normally in use in the textile industry. The following experiments were carried out.

Pyrogenic Activity of Cotton Extracts.—Aqueous cotton extract, 1 ml., prepared at room temperature as indicated by Antweiler (1960) and by Bouhuys, Lindell, and Lundin (1960), when injected intravenously in a rabbit, is strongly pyrogenic. The fever curve has two peaks (Fig. 1) similar to that produced by intravenous injection of endotoxins. The pyrogenic effect was always present when many extracts were used, prepared from different samples of raw cotton and from cotton debris collected in the carding machines. It has been observed, however, that the relative potency of the extracts varied appreciably, the most active extract being that prepared from discarded cotton residues from the carding machines. The extraction of pyrogens from cotton with aqueous solutions is more efficient if the extraction is made at 100° C. instead of at room or ice-box temperature. Extraction with normal saline buffered at *p*H 7·4 at 100° C. for 90 minutes gives an extract about 10 times more pyrogenic than that prepared from the same amount of cotton extracted overnight at room temperature, with the same amount of fluid. This is interesting in that it is similar to the method used by Neter,

* Work of the Section for the Study of Occupational Health in the Textile Industry.

Bertram, Zak, Murdock and Arbesman (1952) for extracting endotoxins from gram-negative bacteria.

The daily intravenous injection of cotton extract produces, in rabbits, a clear-cut tolerance to the pyrogenic effect (Fig. 1), similar to that occurring after daily intravenous injection of endotoxins. More important still is the observation that rabbits made tolerant to the pyrogenic action of cotton extracts are also tolerant to the intravenous injection of purified *S. abortus equi* endotoxin (Fig. 2), and that, on the other hand, animals made tolerant to the endotoxin are tolerant to cotton extracts (Fig. 3). This suggests that the pyrogenic activity of cotton extracts may be due to the presence of endotoxins.

Action of Cotton Extracts on Circulating Leucocytes.—The intravenous injection in the rabbit of 1 ml. of aqueous cotton extract also produces marked variations of circulating leucocytes. First there is a decrease in the number of leucocytes in the peripheral blood, followed by a marked leucocytosis (Fig. 4). Both variations are similar to those elicited by endotoxins (Delaunay, 1943).

Extraction from Cotton of Schwartzmann-active Material.—If the method of Westphal, Lüderitz, and Bister (1952), for the extraction of endotoxins from gram-negative bacteria with phenol solutions, is used for the extraction of cotton samples, variable amounts of water-soluble material are obtained. The amount of extracted material has been 3·3 mg. from 1 g. of raw ordinary cotton (U.S.A. " good middling ") and 9·9 mg. from 1 g. of waste cotton from the carding machines. Chemical analysis showed that in both cases the extracted material

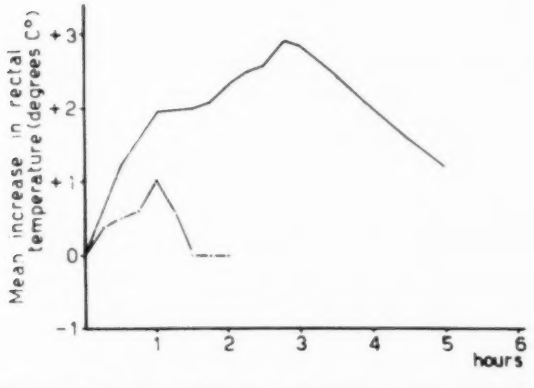

FIG. 1.—Fever patterns induced by 1 ml. intravenous cotton extract in three untreated rabbits (———) and in two rabbits (— · —) after seven days of daily treatment with the same extract.

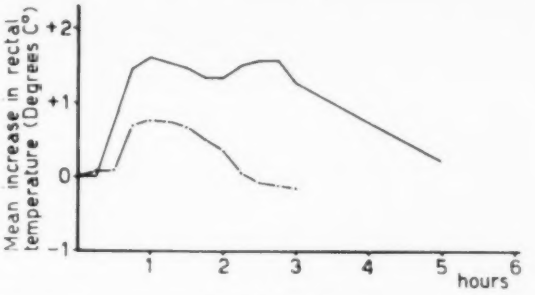

FIG. 2.—Fever patterns induced by 0·05 γ intravenous *S. abortus equi* endotoxin in four untreated rabbits (———) and by 5 γ of the same endotoxin in two rabbits (— · —) injected daily (seven days) with 1 ml. cotton extract.

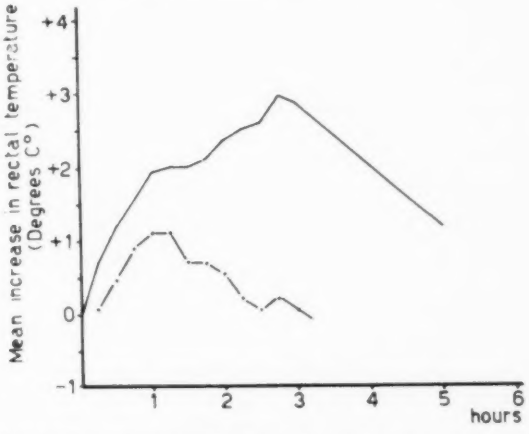

FIG. 3.—Fever patterns induced by 1 ml. intravenous cotton extract in three untreated rabbits (———) and in five rabbits (— · —) made tolerant to 20 γ of *S. abortus equi* endotoxin.

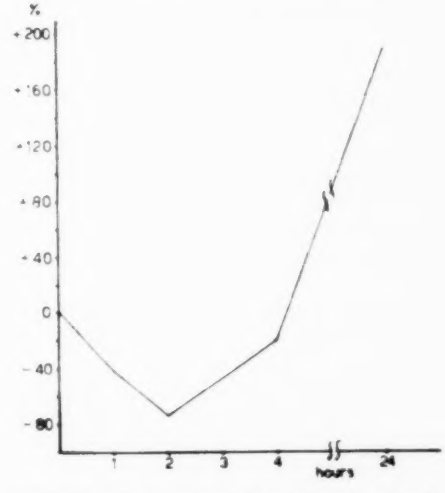

FIG. 4.—Mean value of percentage variations in white blood cell count in three rabbits after intravenous injection of 1 ml. cotton extract.

had a low nitrogen content (1·2% in the first and 3% in the second case) and was comparatively rich in hexoses (17% in both cases).

This material was pyrogenic. The minimal dose capable of increasing the rectal temperature of rabbits by 0·6° C. was 0·2 μg., and it was Schwartzmann active. In fact the intracutaneous injection of 30 μg. of the material extracted from cotton was sufficient to prepare the rabbit for a local Schwartzmann reaction subsequently provoked by the intravenous injection of 50 μg. of purified *E. coli* endotoxin.

Our experiments show consistently the presence, in industrial cotton, of material with biological activities similar to those of the endotoxins of gram-negative bacteria. A rough estimate, based on the pyrogenic activity, indicates that 1 ml. of aqueous cotton extract prepared as indicated by Antweiler (1960) may contain between 10 and 30 μg. of endotoxin-like material (*i.e.* 0·15–0·50 mg. extracted from 1 g. of cotton). A more precise assessment is derived from the extraction of cotton by the method of Westphal, Lüderitz, Eichenberger, and Keiderling (1952). As stated above, this method indicates that 1 g. of waste cotton from the card-rooms may contain about 10 mg. of endotoxin-like material.

We have examined the following samples for the presence of endotoxins: three samples of industrial raw cotton (one " good middling " and one " good ordinary " from the U.S.A. and one of Egyptian cotton), one sample of raw beaten flax, and one of hemp. All these materials contained different amounts of endotoxins, ranging from 3 mg. to 11 mg. per gramme.

It will obviously be useful to determine the endotoxin content of many more samples of cotton of differing grade and origin, and also of other raw natural textile fibres. It is already apparent that the presence of bacterial endotoxins is not limited to some samples of very low-grade cotton, where they have already been shown to be present by Neal, Schneiter, and Caminita (1942).

The origin of the endotoxins found in cotton and other natural textiles can probably be ascribed to the various gram-negative saprophytic bacteria that have developed on the cellulose-rich textiles during the whole period extending from the crop in the fields to processing in the factories. It is reasonable to assume that only a part of these bacteria are still viable in the raw cotton ready for industrial processing. Furness and Maitland (1952) found between 12 and 252 millions of viable gram-negative bacteria (mainly *Aerobacter*) per gramme of different samples of raw cotton. The number of viable gram-negative bacteria found in a sample of cotton or other textiles is not a reliable measure of its endotoxin content, for one must take into account the endotoxins connected with the residues of any dead bacteria that may have remained adhering to the cotton fibres.

One would expect there to be variations in the amount and origin (from different species of gram-negative bacteria) of the endotoxins present in different samples of cotton or other textiles, depending on the varying conditions to which the individual sample is subjected, while still in the crop, during storage and processing. It may be that larger amounts of endotoxins will be found associated with cottons of lower commercial grade that are presumably exposed to more extensive bacterial contamination than the higher grades.

The Relationship between some Experimental Effects of Cotton Extracts and those of Endotoxins

The biological effects of cotton extracts have been studied fairly extensively in experimental animals and in man. Of special interest is the recent work of Bouhuys *et al.* (1960) and of Antweiler (1960), showing the presence in cotton extracts of a substance or substances which are histamine liberators. The demonstration of endotoxins in cotton extracts raises the question as to whether some of the effects observed with cotton extracts, might be due to the endotoxins. Several instances in which this possibility may be considered are listed in Table 1, and will be briefly discussed.

Late Skin Reaction in 90% or More of Normal Subjects.—Cayton, Furness, and Maitland (1952) observed that several cotton extracts, when injected intracutaneously in man, induced a late reaction in almost all subjects. This effect was ascribed by these authors to the presence of a toxic substance, which may have been the endotoxins; it is well known that the intracutaneous injection of very minute amounts of endotoxins induces, after eight to 15 hours, a localized reddening and a slight infiltration in almost all subjects (Thomas, 1954).

Infiltration of Skin with Polymorphonuclear Leucocytes.—Prausnitz (1936) observed, in a self-experiment, that the intradermal injection of several cotton extracts produced a very marked and mainly perivascular infiltration of the dermis by polymorphonuclear leucocytes. A similar reaction was observed in the rabbit. Now this local leucocytic infiltration is one of the characteristic responses to the intradermal injection of endotoxins, and indeed is the morphological basis for the Sanarelli-Schwartzmann phenomenon (Thomas, 1954).

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Fall in peripheral blood pressure and respiratory disturbances in the cat, antagonized by anti-histamine drugs	Bouhuys *et al.* (1960) Antweiler (1960)	Kuida *et al.* (1958) Gilbert (1959)
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Increase in plasma histamine	Antweiler (1960)	Weil and Spink (1957)
Liberation of histamine from heparinized rabbit blood	Antweiler (1960)	Our observation
Fall of circulating platelets	Antweiler (1960)	Davis *et al.* (1960)
Activation of anaphylatoxin in heparinized rat plasma	Our observation	Greisman (1960)
Oedema of the foot-pad in the rat	Antweiler (1960)	Our observation

Primary Toxic Action after Intravascular Injection.—Prausnitz (1936) obtained a toxic material from raw cotton, by aqueous extraction followed by precipitation with ethanol or ammonium sulphate, that proved to be lethal to some guinea-pigs when administered by intravascular injection. Definite anaphylactoid symptoms were observed in the animals. This active material was named " toxic protein " by Prausnitz, although it did not behave chemically as a pure protein. It appears probable that Prausnitz's " toxic protein " contained a fair amount of crude endotoxic protein-lipid-polysaccharide complexes, and that these were responsible for the toxic activity of the preparation.

Fall of Peripheral Blood Pressure and Respiratory Disturbances in the Cat.—These reactions were observed by Bouhuys *et al.* (1960) and by Antweiler (1960) in the anaesthetized cat shortly after an intravenous injection of aqueous cotton extracts. Many workers have observed similar effects in the cat after intravenous injection of endotoxins. Indeed, if the dose of endotoxins is not too high, the action on blood pressure may be inhibited by antihistaminic drugs (Gilbert, 1959), as is the case with cotton extracts.

Liberation of Histamine from the Peritoneal Cavity of the Rat.—This effect was observed by Antweiler (1960) after the intraperitoneal injection of 15 ml. of cotton extract. We have seen a similar liberation of histamine from the peritoneal cavity of rats after 10 ml. Ringer solution containing 50 μg./ml. of endotoxin had been injected intraperitoneally. This liberation occurred with endotoxins from *E. coli*, *S. abortus equi*, and *S. typhi*. This amount of endotoxin is approximately the same as that probably present in 15 ml. of cotton extract.

Increase of Histamine-like Substances in Plasma.—An increase in histamine or histamine-like substances in the plasma of dogs treated with comparatively large amounts of endotoxins has been observed by Weil and Spink (1957). A similar increase of histamine was observed by Antweiler (1960) in the blood of cats treated with cotton extracts.

Liberation of Histamine or Histamine-like Substances from Heparinized Rabbit Blood.—We incubated 2·5 ml. of heparinized (100 μg. heparin/ml.) rabbit blood for 30 minutes at 37° C., with 1 ml. of the following solutions, siliconed glassware being used throughout:

(a) normal saline;

(b) extract from card-room waste cotton prepared in normal saline according to the procedure of Antweiler (1960) and Bouhuys *et al.* (1960);

(c) the same extract filtered through LSG_{60} membrane filters (Membranfilter, Göttingen);

(d) normal saline containing 25 μg./ml. or 50 μg./ml. of *E. coli* endotoxin;

(e) normal saline containing 25 μg./ml. of *S. abortus equi* endotoxin.

After incubation the rabbit blood was centrifuged and 0·25 ml. of the supernatant fluid was transferred to a vessel of 15 ml. capacity containing a segment of terminal guinea-pig ileum. The ileum was immersed in oxygenated Ringer solution and kept at 37° C., a small amount of atropine (1 mg./litre) having been added. The contraction of the guinea-pig ileum was recorded on a revolving drum. The results of a typical experiment are shown in Fig. 5. They confirm the observation of Antweiler (1960) concerning the ability of crude cotton extracts to liberate histamine or histamine-like substances from whole heparinized rabbit blood.

Fig. 5 shows, moreover, that the active substance or substances in cotton extracts are mainly withheld by Membranfilters LSG_{60} which do not allow the passage of molecules of molecular weight appreciably greater than 10,000.

They also show that histamine or histamine-like substances (contraction of the ileum inhibited by 1 μg./ml. of pyribenzamine) are liberated by incubation of heparinized rabbit blood with *E. coli*

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Oedema of the foot-pad in the rat	Antweiler (1960)	Our observation

Primary Toxic Action after Intravascular Injection.—Prausnitz (1936) obtained a toxic material from raw cotton, by aqueous extraction followed by precipitation with ethanol or ammonium sulphate, that proved to be lethal to some guinea-pigs when administered by intravascular injection. Definite anaphylactoid symptoms were observed in the animals. This active material was named "toxic protein" by Prausnitz, although it did not behave chemically as a pure protein. It appears probable that Prausnitz's "toxic protein" contained a fair amount of crude endotoxic protein-lipid-polysaccharide complexes, and that these were responsible for the toxic activity of the preparation.

Fall of Peripheral Blood Pressure and Respiratory Disturbances in the Cat.—These reactions were observed by Bouhuys *et al.* (1960) and by Antweiler (1960) in the anaesthetized cat shortly after an intravenous injection of aqueous cotton extracts. Many workers have observed similar effects in the cat after intravenous injection of endotoxins. Indeed, if the dose of endotoxins is not too high, the action on blood pressure may be inhibited by antihistaminic drugs (Gilbert, 1959), as is the case with cotton extracts.

Liberation of Histamine from the Peritoneal Cavity of the Rat.—This effect was observed by Antweiler (1960) after the intraperitoneal injection of 15 ml. of cotton extract. We have seen a similar liberation of histamine from the peritoneal cavity of rats after 10 ml. Ringer solution containing 50 μg./ml. of endotoxin had been injected intraperitoneally. This liberation occurred with endotoxins from *E. coli*, *S. abortus equi*, and *S. typhi*. This amount of endotoxin is approximately the same as that probably present in 15 ml. of cotton extract.

Increase of Histamine-like Substances in Plasma.—An increase in histamine or histamine-like substances in the plasma of dogs treated with comparatively large amounts of endotoxins has been observed by Weil and Spink (1957). A similar increase of histamine was observed by Antweiler (1960) in the blood of cats treated with cotton extracts.

Liberation of Histamine or Histamine-like Substances from Heparinized Rabbit Blood.—We incubated 2·5 ml. of heparinized (100 μg. heparin/ml.) rabbit blood for 30 minutes at 37°C., with 1 ml. of the following solutions, siliconed glassware being used throughout:

(a) normal saline;

(b) extract from card-room waste cotton prepared in normal saline according to the procedure of Antweiler (1960) and Bouhuys *et al.* (1960);

(c) the same extract filtered through LSG_{60} membrane filters (Membranfilter, Göttingen);

(d) normal saline containing 25 μg./ml. or 50 μg./ml. of *E. coli* endotoxin;

(e) normal saline containing 25 μg./ml. of *S. abortus equi* endotoxin.

After incubation the rabbit blood was centrifuged and 0·25 ml. of the supernatant fluid was transferred to a vessel of 15 ml. capacity containing a segment of terminal guinea-pig ileum. The ileum was immersed in oxygenated Ringer solution and kept at 37° C., a small amount of atropine (1 mg./litre) having been added. The contraction of the guinea-pig ileum was recorded on a revolving drum. The results of a typical experiment are shown in Fig. 5. They confirm the observation of Antweiler (1960) concerning the ability of crude cotton extracts to liberate histamine or histamine-like substances from whole heparinized rabbit blood.

Fig. 5 shows, moreover, that the active substance or substances in cotton extracts are mainly withheld by Membranfilters LSG_{60} which do not allow the passage of molecules of molecular weight appreciably greater than 10,000.

They also show that histamine or histamine-like substances (contraction of the ileum inhibited by 1 μg./ml. of pyribenzamine) are liberated by incubation of heparinized rabbit blood with *E. coli*

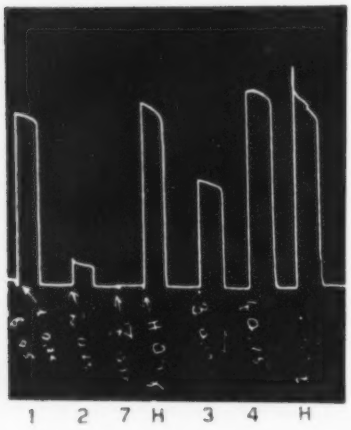

FIG. 5.—Action on the isolated guinea-pig ileum of supernatant from heparinized rabbit blood incubated (2·5 ml. blood + 1 ml. indicated solution/litre) with:
(1) Cotton extract (crude) in saline;
(2) Cotton extract filtered through Membranfilter LSG_{60};
(3) *E. coli* endotoxin in saline, 25 γ/ml.;
(4) *E. coli* endotoxin in saline 50 γ/ml.;
(7) Normal saline;
H = 0·5 γ histamine.

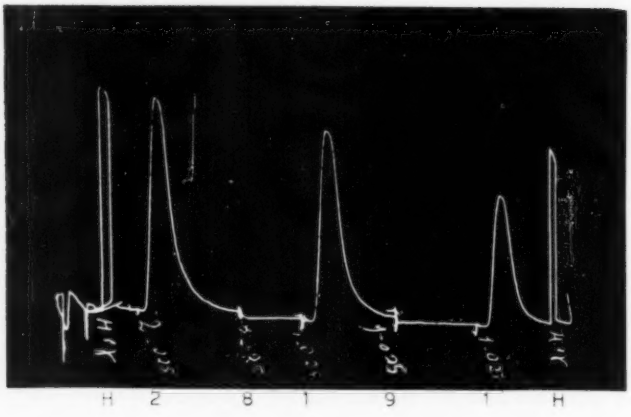

FIG. 6.—Action on the isolated guinea-pig ileum of heparinized rat plasma incubated with equal amounts of:
(1) Agar (Difco) 0·1 mg./ml. normal saline;
(2) Cotton extract (crude) in normal saline;
(8) Normal saline;
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Fall of Circulating Platelets.—Antweiler (1960) showed that the intravenous injection of cotton extracts produced a marked fall of circulating platelets in the rabbit. This might be due to the endotoxins present in cotton extracts in view of the dramatic reduction of blood platelets after the intravenous injection of purified endotoxins (Davis, Meeker, and McQuarrie, 1960).

Activation of Anaphylatoxin in Heparinized Rat Plasma.—Greisman (1960) has shown that activation of anaphylatoxin can be achieved by incubating fresh heparinized rat plasma with small amounts of *E. coli* endotoxin. To find out whether a similar effect might be obtained with cotton extracts, we incubated different crude cotton extracts in normal saline for 30 minutes at 37° C., prepared as indicated by Antweiler (1960), with equal amounts of fresh heparinized (100 μg./ml.) rat plasma. After incubation the presence of activated anaphylatoxin in the rat plasma was investigated by its action on freshly prepared guinea-pig ileum as indicated by Rothschild and Rocha e Silva (1954).

The results of a typical experiment show that rat plasma anaphylatoxin can be activated by a crude cotton extract (Fig. 6). As was to be expected no anaphylatoxin activation was obtained with a solution of compound 48/80. The anaphylatoxin experiment thus demonstrates one instance in which the histamine liberating activity of cotton extracts is comparable with that of endotoxins, and different from that of low molecular weight histamine liberators such as compound 48/80.

That the anaphylatoxin activating substance (or substances) of cotton extracts are molecules of considerable size is shown by the complete inactivity of filtrates passed through LSG_{60} Membranfilters.

Oedema of the Foot-pad in the Rat.—A further similarity between the action of cotton extracts and that of endotoxins is shown by the ability of both to induce the rapid production of oedema in the foot-pad of the rat. Antweiler (1960) demonstrated this for cotton extracts, and we have shown that the injection of 50 μg. *E. coli* endotoxin dissolved in 0·1 ml. saline and injected into the dorsal side of the foot-pad of the rat induces, after 20 to 30 minutes, a marked oedematous swelling. If the animal had previously received an intracardiac injection of 1 ml. of a 1% Evans blue solution in saline, then the oedematous zone stained blue, due to the free passage of the Evans blue molecules through capillaries whose permeability was abnormally high.

The above facts and considerations suggest that in evaluating the pharmacological effects of cotton extracts their endotoxin content must be considered. They certainly do not prove that all the biological activity of cotton extracts is due to

endotoxins. Indeed, there is some evidence against this hypothesis. For instance, the ability of cotton extracts to liberate histamine from whole heparinized rabbit blood seems to be appreciably greater than that produced by their endotoxin content. Furthermore this ability is not entirely abolished (Fig. 5) by the filtration of cotton extracts through LSG_{60} Membranfilters, which should retain all the endotoxins. It is quite reasonable to assume that crude cotton extracts might contain other pharmacologically active substances (including histamine liberators) which are different from the endotoxins. The nature of these hypothetical substances is not known but it will not be surprising if crude cotton extracts are shown to contain various polysaccharides generally similar, at least in their ability to liberate histamine, to the glucose polymer dextran. It is of interest that even dextrans of comparatively low molecular weight (down to 14,000) retain their ability to liberate histamine from heparinized rabbit blood (Haining, 1955).

Effects of Inhalation of purified Endotoxins or Cotton Extracts—Experiments on Rabbits

A crucial point in our work is the assumption that endotoxins are active if absorbed by inhalation and that their action is similar to that of inhaled cotton dusts or extracts. To investigate this point we have given healthy hybrid rabbits (1·5 to 2 kg. body weight) of both sexes aerosol inhalations of purified endotoxins or cotton extracts.

Inhalation of Endotoxins.—Many experiments were performed on a total of 43 animals, with different doses and different kinds of endotoxins administered at different intervals, but they need not be reported here in detail. It is sufficient to say that in most experiments the animals were made to inhale an aerosol of a solution containing 15 μg./ml. *S. abortus equi* endotoxin in saline for 15 minutes. During these 15 minutes 4 ml. of the solution were aerosolized, an unknown amount of solution being actually absorbed by the animals.

The main effect of this inhalation was the appearance of fever and dyspnoea in a variable percentage of the animals (Fig. 7). The fever response was usually equivalent to an increase in rectal temperature of 1 to 1·5° C. The dyspnoea was often clearly evident and was recorded with spirographic tracings (Fig. 8a and b). Both fever and dyspnoea were usually observed from 30 to 50 minutes after the end of the inhalation.

Both fever and dyspnoea appeared occasionally after the first inhalation of endotoxins, but became more frequent after the second, third, and so on. Fever or dyspnoea only appeared if the new inhalation was performed after an interval of some days from the preceding one. If the inhalations took place on two consecutive days, then the second one of the two was consistently without effect, regardless of the previous exposure of the individual rabbit and of its tendency to respond with fever and dyspnoea. This is presumably due to the well-known phenomenon of tolerance to the endotoxins, and is reminiscent of the Monday effect which is characteristic of many diseases connected with the inhalation of textile or other vegetable dusts.

Inhalation of Cotton Extracts.—The animals inhaled a crude cotton extract in saline prepared as indicated by Antweiler (1960). Neither fever nor dyspnoea was ever observed after this treatment, and this is in accord with the previous observations of Neal *et al.* (1942) who did not observe in different animals (including rabbits) symptoms that the inhalation of cotton dust or extracts readily produced in man and baboons. If, however, rabbits previously "sensitized" by inhalation of endotoxins were exposed to the inhalation of cotton

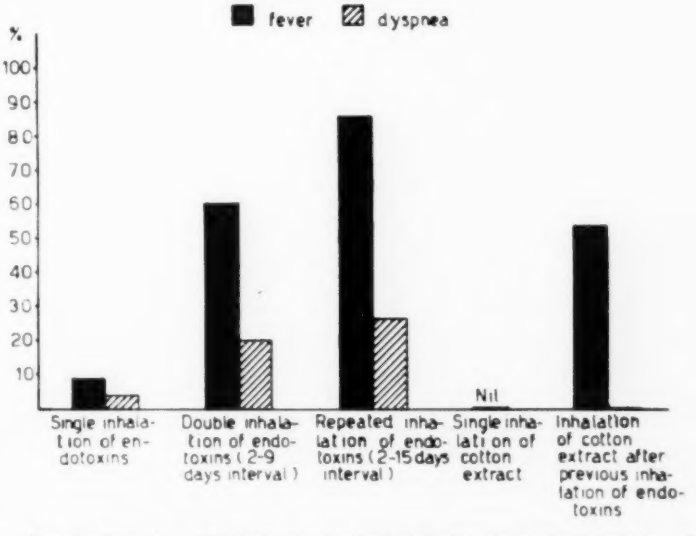
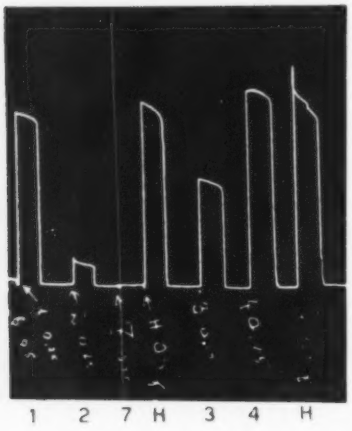


FIG. 7.—Percentage of rabbits showing indicated alterations after inhalation of endotoxins or cotton extracts.



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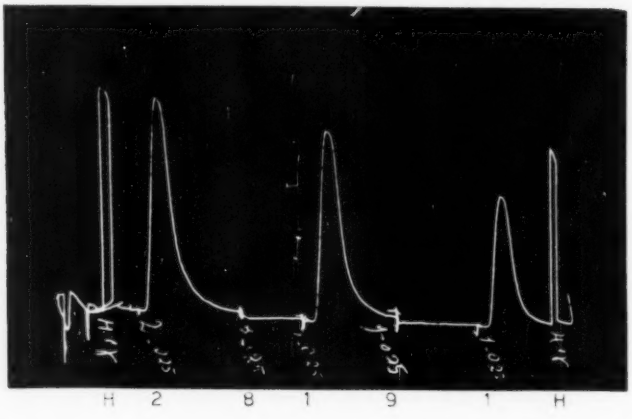

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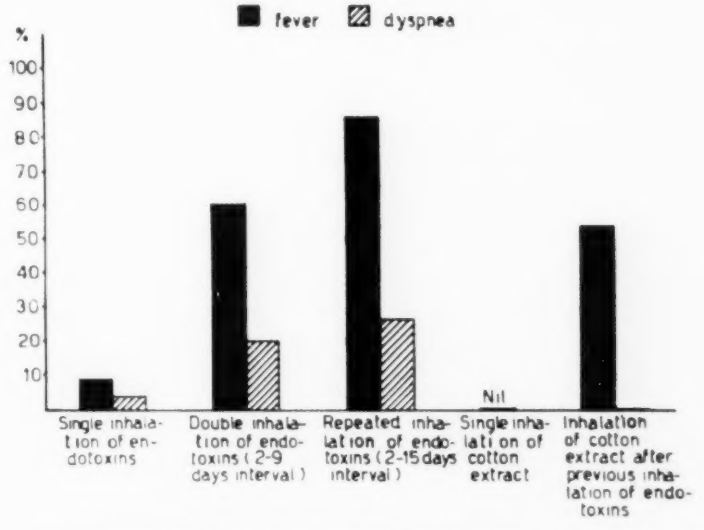

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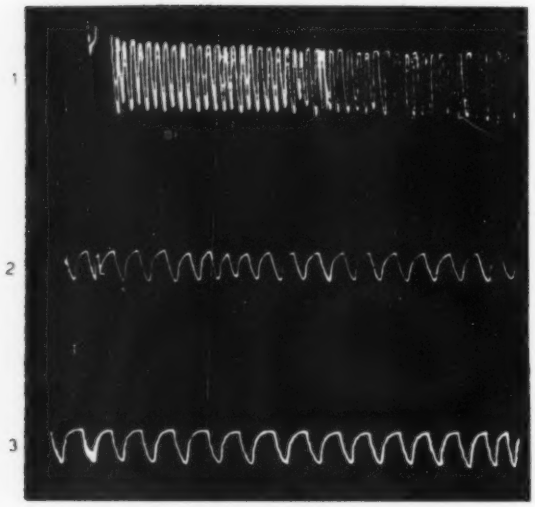

FIG. 8a.—Spirogram of rabbit No. 56
1 = untreated; 2 = 30 min. after second inhalation of endotoxin aerosol (50 γ/ml.); 3 = 60 min. after.

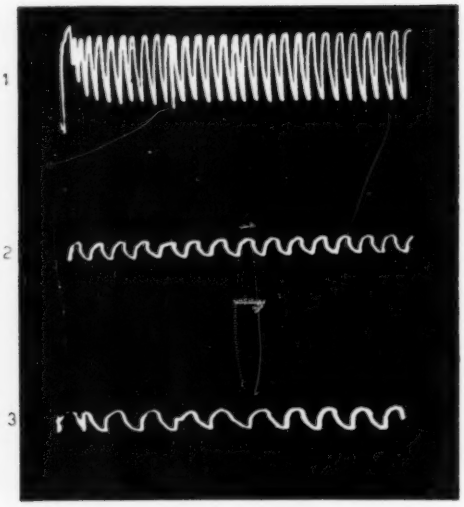

FIG. 8b.—Spirogram of rabbit No. 23
1 = untreated; 2 = 30 min. after the sixth inhalation of endotoxin aerosol (35 γ/ml.); 3 = 60 min. after.

extract after a suitable interval, a substantial number of them showed fever (Fig. 7). The effect of repeated and suitably spaced inhalations of cotton extracts alone has not yet been investigated.

Inhalation of Endotoxins; Experiments on Man

Neal *et al.* (1942) gave a brief description of the effects observed in a subject who was exposed to the inhalation of an aerosol made from the sterile filtrate of a culture of *Aerobacter cloacae*, a gram-negative bacterium known to produce an endotoxin. About 45 minutes after the end of the inhalation they observed the onset of fever, cough, dyspnoea, diffuse aches and nausea. We inhaled aerosols of purified endotoxins. In the first experiment three of us inhaled about 3 ml. of saline containing 5·10 and 20 μg./ml. of *E. coli* endotoxins respectively. The immediate effects were dry coughing and shortness of breath, accompanied by a slight reduction of the one second timed vital capacity, measured with a spirometer by the method of Tiffeneau and Drutel (1952). After four days two of the subjects again inhaled 3 ml. of an aerosol of a solution containing 20 μg./ml. of *S. abortus equi* endotoxin; the symptoms were the same with the addition of slight fever (to 37·5° C.) and a definite feeling of malaise. The third subject, who had inhaled only the 10 μg./ml. dose of *E. coli* endotoxin, had developed (probably because of a condition of hypersensitivity), a severe reaction with a diffuse skin rash and high fever, and this prompted the discontinuation of the experiments. An investigation of the possible effects of inhalation of endotoxins was then undertaken amongst the workers in a pharmacological firm in Milan where typhoid vaccines were manufactured. We found that while the centrifuging killed *S. typhi* (an operation performed about once every three months involving the centrifuging of considerable amounts of bacterial suspensions in a Sharples centrifuge) the conditions were sometimes such that an appreciable quantity of bacteria was dispersed in the air and subsequently inhaled by the workers. Amongst these the onset of fever (to 39·5° C.) was then regularly observed, and one of the workers had also shown a diffuse scarlatiform skin rash on one occasion. But the most interesting fact was that all the subjects with spontaneous bronchial affections, and especially those with a history of chronic bronchitis, had to be excluded from the rooms where the typhoid vaccine was manufactured because they often had asthmatic attacks, especially when centrifuging bacterial suspensions.

Occupational Diseases in the Pathogenesis of which Endotoxins appear to Play a Part

Inhaled endotoxins may have a role in the pathogenesis of occupational diseases connected with the inhalation of vegetable dusts. These diseases often appear in small epidemics and display a somewhat uniform symptomatology, the main symptoms being attacks of fever, coughing,

dyspnoea, headache, nausea, diffuse aches, and malaise. These symptoms are strikingly similar to the effects of endotoxins. Usually, there is no alteration in the chest radiograph and recovery is complete within one or two days. In some instances, however, such as " farmer's lung " and bagassosis a mottling often appears in the chest radiograph and recovery may take weeks to complete. This may be due to the inhalation of larger amounts of endotoxins. When exposure to the inhalation of vegetable dusts is repeated daily, as with many workers in the textile industry, the symptoms usually appear, or are more severe, upon resuming work after one or more days of absence, such as on Mondays.

Table 2 gives a synopsis of the occupational diseases that we believe may be connected with the inhalation of endotoxins.

The main symptoms of these diseases bear a superficial resemblance to those of the allergic reactions of the asthma–hay fever group with which they have often been included. We feel, however, that this inclusion is not justified. In fact, a specific hypersensitivity for a given antigen has never been conclusively shown in any of the diseases listed in Table 2, neither with skin tests nor with other immunological methods. Moreover these diseases generally involve numerous subjects who are engaged in the same work and seem to be connected with the inhalation of considerable amounts of the noxious substances, while the allergic conditions of the asthma–hay fever type are associated with the peculiar reactivity of some individuals and are elicited by contact with minimal amounts of the specific allergen. Also, as has been pointed out by Schilling (1956), the tolerance phenomenon that gives the characteristic Monday effect is not observed in cases of allergic asthma, even if this has an occupational origin.

It is more reasonable to assume that the vegetable dusts listed in Table 2 all contain, or are contaminated with, a toxic substance or substances whose biological effects are similar to the symptoms of an allergic reaction; thus we agree with Bouhuys *et al.* (1960) and with Antweiler (1960) whose work has shown that cotton dusts in textile mills contain a toxic substance or substances which are histamine liberators. We believe that at least part of the histamine-liberating activity of cotton extracts is due to their endotoxin content.

Thus the pharmacological activity of cotton extracts is mainly due to contamination with bacterial substances and not to a product of cotton itself. Indeed the fact that active substances capable of inducing similar pathological reactions in man are apparently present in various vegetable materials deriving from taxonomically different plants such as cotton, sugar cane, grain, malt, flax, hemp, and others, is by itself suggestive that the origin of these active substances is probably due to a contaminant. Also occupational diseases very similar to the so-called " mill fever " or " Monday fever " of cotton workers, have been observed amongst operatives who had never been exposed to cotton or other textile dusts, but who were certainly exposed to the inhalation of endotoxins. In fact it appears that cases of Monday fever are not rare amongst the personnel of

TABLE 2

SYNOPSIS OF OCCUPATIONAL DISEASES POSSIBLY DUE TO THE INHALATION OF ENDOTOXINS

No.	Disease	Origin	Affected Workers	Monday Effect	Described by
1	Mill fever (Monday fever)	Cotton	New card-room or other cotton workers—endemic	+	Many authors since 1784
1 (a)	Byssinosis	Cotton	Old card-room workers	+	Many authors
2	Weaver's cough	Cotton	Weavers—epidemic		Collis (1915) Middleton (1926) Vigliani *et al.* (1954)
3	Mattress maker's fever	Low-grade cotton	Mattress makers—epidemic, severe		Neal *et al.* (1942) (endotoxin role ascertained)
4	Hemp fever	Hemp	Hemp beaters—endemic	+	
5	Hackling fever	Flax		+	
6	Grain fever	Grain	Silo workers		
7	Malt fever	Malt			
8	Bagassosis	Bagasse (sugar cane)	Bagasse workers—endemic, severe		Role of endotoxins ascertained by Schneiter *et al.* (1948)
9	Farmer's lung or Thresher's lung or Harvester's lung	Hay	Farmers—endemic, severe		Many authors; see Frank (1958)
10	Bible printer's fever	Humidifier + cellulose dust	Printers—epidemic	+	Contamination with gram-negative bacteria and role of endotoxins ascertained by Tejning and Grubb (1959)
11	Befeuchterungsanlage Fieber	Humidifier + sawdust	Wood model makers—epidemic	+	Pestalozzi (1959)

laboratories continuously engaged in the extraction and purification of endotoxins (Westphal, 1959).

Tejning and Grubb (1959) observed a small epidemic of " Monday fever " amongst printers working in a room equipped with an humidifier in which the water had become contaminated with gram-negative bacteria and contained endotoxins. An almost identical observation had previously been made by Pestalozzi (1959) in a Swiss factory manufacturing wood models. Pestalozzi ascribed the cause of attacks of fever and coughing occurring on Mondays to the contamination of the water of an humidifier (" befeuchters Fieber "), but he did not perform a complete bacteriological analysis of the contaminated water and thought that moulds were the cause of the disease, through an allergic mechanism. That bagassosis and a peculiar epidemic of fever and coughing observed amongst workers handling very low grade cotton for making mattresses were indeed due to endotoxins was demonstrated by Schneiter, Reinhart and Caminita (1948) and by Neal *et al.* (1942). Our demonstration of the constant presence of endotoxins in cotton supports the thesis that the diseases of cotton operatives showing fever and cough (mill fever, weaver's cough) are also due to the endotoxins. In weaver's cough it is necessary to consider the presence of endotoxins not only in the cotton itself, but also in the size in which the threads are immersed before weaving. The process of sizing, performed in aqueous solutions at high temperature, might dissolve a good deal of endotoxins from the bacterial bodies, a process which is similar to the extraction of endotoxins with hot aqueous buffers (Neter *et al.*, 1952). Thus the sized threads might even be sterile, in so far as viable bacteria are concerned, but still be rich in the endotoxins that have dried on them. This agrees with the facts observed by one of us (Vigliani, Parmeggiani, and Sassi, 1954) in an epidemic of " weaver's cough ".

There is no doubt that in weaver's cough, as in other instances, contamination of cotton or other materials is not restricted to gram-negative bacteria; yet we claim that the products of the gram-negative bacteria play a major role in the pathogenesis of the diseases because the observed symptoms and the Monday effect match well with the known effects of endotoxins.

Moulds are among the main contaminants of many cellulose-rich materials, particularly if moist, and to them or to their products some authors have ascribed the aetiology of certain occupational diseases connected with the inhalation of vegetable dusts (for example, farmer's lung, weaver's cough, and " befeuchters Fieber "). However, no proof of this assumption has been given, and we wish to point out that moist cellulose-rich materials not only favour the development of moulds, but also of gram-negative bacteria of the aerogenes-capsulatus group that are often able to ferment the polysaccharides.

The Problem of Byssinosis.—The differences that exist between byssinosis and the diseases of the " mill fever " group, have been pointed out by Schilling (1956). Two of these differences, namely the absence of fever in byssinosis and the fact that years of exposure to cotton dust appear necessary for byssinosis to occur, are not easily reconciled with the hypothesis that endotoxins play a major role in the pathogenesis of byssinosis. On the other hand the patients affected by byssinosis in the earlier stages of the disease show a typical tolerance to the effects of the materials inhaled in the cotton factories, because they are worse on Monday as are those affected by mill fever or similar diseases. It may be, as already indicated by Neal *et al.* (1942), that byssinosis is due to protracted inhalation of small amounts of endotoxins.

This might result in a condition of immunological hypersensitivity, retaining some of the aspects of the reaction to endotoxins, such as tolerance.

More experimental work, coupled with observations on man, will be necessary in order to test this possibility.

The authors are grateful to Prof. O. Westphal of the Wander Forschungs Institut, Freiburg-i-B., for a generous gift of purified *E. coli* endotoxin (from 2 *coli* 0 111), to Dr. E. Eichenberger, of the Wander Research Laboratories, Bern, Switzerland, who provided the *S. abortus equi* endotoxin and to Dr. G. Di Nardo, of the Institute of Microbiology of the University of Milan, who kindly prepared the lipopolisaccharide from *S. typhi* 0 901.

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Addendum

It is interesting to point out that Paine (1946) observed, in four subjects exposed to the experimental inhalation of "*Serratia marcescens*", the appearance of an acute illness with coughing and fever. He ascribed these symptoms to the endotoxin of "*Serratia marcescens*".

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Brit. J. industr. Med., 1961, **18**, 130.

HISTAMINE LIBERATION BY COTTON DUST EXTRACTS: EVIDENCE AGAINST ITS CAUSATION BY BACTERIAL ENDOTOXINS

BY

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The recently stated hypothesis that histamine liberation by cotton dust extracts is caused by endotoxins from gram-negative bacteria contained in cotton was studied experimentally in various animals. It was shown clearly that such amounts of endotoxin as were found in cotton dust did not give rise to histamine liberation which was provoked by extracts from cotton card-room dusts. Further arguments are given which testify against the endotoxin hypothesis.

We have recently shown in various animal experiments that aqueous extracts of several cotton materials (raw cotton, card-room dust, and shreds from the carding machines) and extracts of certain parts of the cotton plant (leaves, stem, and seed capsule fragments) contain a histamine-liberating factor. The biological activity of this factor is much greater than that of the actual histamine content of the dusts or plant tissues used (Antweiler, 1959a; 1960a, b, c). Thus, for the first time, we can furnish evidence in favour of the hypothesis put forward by Haworth and Macdonald (1937) and recently by Bouhuys (1959) and Bouhuys, Lindell, and Lundin (1960).

From the results of these experiments we infer that there may be a relationship between the histamine-liberating factor in cotton dust and the dyspnoeic Monday feeling of card-room workers, recently described by Schilling (1956, 1960) and Roach and Schilling (1960). The chemical nature of the histamine-liberating factor which is heat-resistant and passes protein-tight membrane filters is still unknown.

Pernis (1960) has recently confirmed our findings. Moreover, he has succeeded in producing anaphylatoxin by incubating rat plasma with cotton dust extracts and has observed a pyrogenic effect after intravenous injection of cotton extract in rabbits. By comparing the phenomena brought about in animals by parenteral application of cotton extracts with the similar action of endotoxins of gram-negative bacteria (*E. coli*, *S. abort. equi*, *S. typhi*, *Aerobacter cloacae*) described in the literature, Pernis concluded that the histamine-liberating factor of cotton extracts might be due to the presence of the endotoxins of bacteria, found in the raw cotton used in cotton-spinning.

In cotton dust samples from America and India which liberate histamine, we had found aerobe spore bacteria such as *B. subtilis*, *B. megaterium* and *B. cereum* and also fungi like *Asperg. niger* and *A. flavus*. Using homogenates of cultures from these bacteria we could not observe any histamine liberation in our animal experiments. We thought therefore that the histamine release caused by cotton extracts was not produced by bacteria or bacterial substances.

Because of Pernis' hypothesis we undertook some experiments to find out whether well-known endotoxins induce rapid histamine liberation when they are employed in such quantities as might be contained in industrial cotton dusts or cotton plant fragments.

Experimental Methods

We chose the endotoxins from *S. abort. equi* (Pyrexal) and from *E. coli* 0111 (Dr. A. Wander Forschungsinstitut). The experimental methods were the same as we had used earlier (Antweiler, 1960a) in proving histamine liberation by cotton extracts. We injected the endotoxins intraperitoneally into rats and looked for microscopical variations of the mast cells of the mesentery and determined the amount of histamine present in the abdominal fluid. Heparinized rabbit blood was incubated at 37° C. with the endotoxins, and afterwards we tested the histamine content of the plasma. The endotoxin

action on blood pressure and respiration of anaesthetized cats was examined.

The endotoxins were dissolved in physiological saline to the same dilutions as used in the cotton extract experiments. All other details of the experimental procedures (animals, time relations, temperature, fixation and staining, and recording) were similar to our former trials. The histamine content was assayed on isolated and atropinized (10^{-7} atropine sulphate) guinea-pig ileum, suspended in aerated tyrode-solution at 30° C., and compared by adding a standard solution of histamine-dihydrochloride (10^{-5}).

We also tried to verify the anaphylatoxic potency of cotton dust extracts in rat plasma and to compare this activity with the proportion of anaphylatoxin elicited by endotoxins. For this purpose we incubated 2 volumes of rat plasma with 1 volume of cotton card-room dust extract and endotoxin respectively in tyrode-solution during 30 min. at 37° C. Endotoxin from *S. abort. equi* was added in a dose of 0·5 μg. and the *E. coli*-endotoxin in doses of 1 μg., 10 μg., and 100 μg. to every 3 ml. of rat plasma. In some experiments we also tested the anaphylatoxic activity of different samples of dry cotton, wool, and some mineral substances. The anaphylatoxin formation by dextran (20 mg.) served as a comparable standard. In order to be certain that the anaphylatoxic activity of cotton dust extracts was not produced by the histamine known to be present in cotton dust, we tested the activity of equal doses of cotton extracts with and without rat plasma incubation.

Results

Examining the effect of the two endotoxins in concentrations of 0·1 to 10·0 μg. in 20 ml. tyrode-solution two hours after injection into the peritoneal cavity of rats, we were unable to detect any noticeable mast cell destruction or change of metachromatic staining of these cells. When withdrawn 20 minutes after administration, it was shown by testing it on guinea-pig ileum that there was no release of histamine in the peritoneal fluid.

After incubation of 5 ml. of rabbit blood with 0·1–1·0 μg. of endotoxin from *S. abort. equi* or with 0·1–10·0 μg. of *E. coli*-endotoxin at 37° C. for 10 minutes, no increase of plasma histamine was found as compared with the control samples incubated only with tyrode-solution.

When 0·1, 1·0 or 2·0 μg. of endotoxin from *S. abort. equi* or 1·0 to 10·0 μg. of *coli*-endotoxin/kg. body weight were injected intravenously in chloralose-urethane anaesthetized cats, there was no delayed, profound and sustained fall in arterial blood pressure, as is always evoked by the histamine liberator 48/80 or by extracts of cotton card-room dusts. Even when the examination was continued for 30 minutes, no definite changes in blood pressure were observed. The recording of respiratory volumes by the method of Konzett-Rössler also yielded no variation after injection of endotoxins.

In testing the activation of anaphylatoxin in rat plasma by incubation with endotoxins, it was noticed that 100 μg. of *coli*-endotoxin caused a weaker activation of anaphylatoxin than an extract from only 200 mg. cotton card-room dust. This amount of 100 μg. of endotoxin corresponds to nearly 50–100 mg. of dried bacteria, but there cannot be this quantity of bacteria in 200 mg. of cotton dust.

Boiling of acidified cotton extracts (*p*H 3) for 30 minutes did not influence the anaphylatoxic activity when tested after neutralization. Endotoxin solutions, on the contrary, lost their activity completely by this procedure.

The other materials examined for anaphylatoxic potency (dry clean cotton and wool and mineral dusts, *i.e.* quartz, rock crystal, quartz glass, Kieselguhr, titandioxide) yielded negative results. Dry raw cotton dust mixed with rat plasma produced the same activity as cotton dust extracts containing an equal quantity of cotton dust.

Discussion

It is well known that much larger doses of endotoxins than we used induce the shock syndrome with acute fall of blood pressure and disturbance of respiration when they are given by intravenous injection to cats (Gilbert, 1959) or dogs (Davis, Meeker, and McQuarrie, 1960). These effects are probably caused by rapid histamine liberation (Greisman, 1960). The doses of endotoxins used by these authors (1·0–10·0 mg./kg. body weight) were considerably greater than the amounts which could be contained in our cotton dust extracts, the active extract doses of which corresponded to 200–400 mg. dust. These quantities of dust cannot possibly contain as much as 1 mg. endotoxin. The water content of bacteria is 80–90% and the dust would have to contain 50 to 100 mg. of dry bacterial substance, since the amount of endotoxin in dried bacteria is only 1–2%.

There is still another argument which testifies against the endotoxin nature of the histamine-liberating factor in cotton dust, namely, that boiling an acidified cotton extract does not lower its activity as an anaphylatoxin producer. Endotoxin solutions, however, do lose their activity by this procedure. Furthermore, it would not be compatible with the endotoxin hypothesis that the different parts of the cotton plant contain different amounts of the histamine-liberating factor, especially as those plant tissues which are most contaminated by handling, that is, cotton hairs, have no histamine-liberating activity. Also it does not seem reasonable to suppose that endotoxins of gram-negative bacteria are only allied with cotton dust and not with other dusts of similar physical and chemical character.

Finally it must be pointed out that the symptoms after inhalation of cotton card-room dust in man (tightness of the chest, cough, and breathlessness) are not the same as the responses after application of endotoxins. For example, fever seldom occurs in cotton workers with severe Monday feeling (Müller, 1959), whereas endotoxins (" pyrogens ") always cause fever whenever they cause substantial symptoms.

We think, now as before, that the histamine-liberating factor in cotton dust is essentially bound to a pharmacologically active substance of the cotton plant itself. It is noteworthy that other naturally occurring substances such as cowhage from *Mucuna pruriens* (Broadbent, 1953), thalassine from sea anemone (Jaques and Schachter, 1954) and flax (Antweiler, 1959b) contain histamine liberators.

I am greatly indebted to Professor O. Westphal of the Dr. A. Wander Forschungsinstitut for supplying purified endotoxin from *E. coli* 0·111 and for his advice in the preparation of endotoxin solutions. I wish to thank Dr. E. Hirsch (of the bacteriological department of Rheinpreussen AG) very much for isolating, identifying, and culturing the micro-organisms in cotton dust. For technical assistance I am grateful to Mrs. Karentz and Mrs. Müller.

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CHRONIC PULMONARY BERYLLIOSIS IN A FEMALE CHEMIST

BY

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A chronic progressive granulomatous disease of the lungs is described in a female chemist who worked for about two years with a beryllium compound in the manufacture of fluorescent lighting tubes. The level of beryllium in the laboratory atmosphere was found to be 2·7 μg. per cu.m. and in other parts of the factory up to 39·1 μg. per cu.m. were recorded. Symptoms began about two years after she left this work and she died three years later. A diagnosis of chronic pulmonary berylliosis was made, and confirmation was obtained by lung biopsy when early in the course of the disease a large cyst attached to the right middle lobe was removed by thoracotomy. Tests of lung function showed that there was a low arterial saturation at rest and a normal P_{CO_2} in spite of marked hyperventilation. Both elastance and resistance of the lungs were greater than normal and total work of breathing was six times the normal. Pregnancy was associated with relief of symptoms which persisted for some months after a normal birth. Death occurred about seven years after exposure to beryllium ceased. At necropsy beryllium was detected in the lungs chemically and demonstrated in histological sections by special stains. Microscopic examination of the lung showed conchoidal bodies and doubly refractile crystals and the pathogenesis of these lesions is discussed. It is suggested that there is a sensitivity reaction to beryllium, which is probably combined with protein to form an antigen, and that the breakdown of necrotic foci provokes a further reaction in the lung with the repeated appearance of fresh lesions.

Chronic beryllium granuloma of the lungs is a rare disease in the United Kingdom and only six case reports have been published (Agate, 1948; Sneddon, 1955, 1958; Rogers, 1957; Jordan and Darke, 1958; Wood, Ball, and Teare, 1958).

A further example from the United Kingdom of a patient with beryllium granuloma of the lungs is now presented, together with a necropsy report. A brief report of this case was given to the Pathological Society of Great Britain and Ireland (Rannie, 1956).

Case Report

In December 1952, a 27-year-old married female chemist attended hospital, complaining of recent breathlessness on exertion and a productive cough. A radiograph of the lungs suggested miliary tuberculosis (Fig. 2), although no tubercle bacilli were found in the sputum. At New Bridge Street Chest Clinic, Newcastle upon Tyne, it was discovered that between 1948 and 1950 she had handled material containing beryllium in a fluorescent lamp factory and that in July 1949 a chest radiograph had been taken which was normal (Fig. 1). Further investigations were carried out in Walker Gate Hospital (Table 1), where the urine was examined for beryllium without success. A cyst in the right lung which had been present when she was radiographed in December 1952 began to increase in size early in 1953 (Fig. 3), and breathlessness became so marked that it was removed.

This was done at the Newcastle Regional Chest Surgery Centre at Shotley Bridge by Mr. W. C. Barnsley, and the investigations made at this time are also shown in Table 1.

The cyst lay between the right middle and lower lobes and was attached to the lower aspect of the right middle lobe by a small pedicle of lung tissue (Fig. 4). The right lung was solid looking and difficult to inflate, its surface was studded with fine hard nodules, and it felt granular. There were some firm lymph nodes in the right hilum.

The histology of the cyst, some lung tissue attached to it, and some hilar lymph nodes, were reported on by Dr. J. D. McGregor of the Pathology Department,

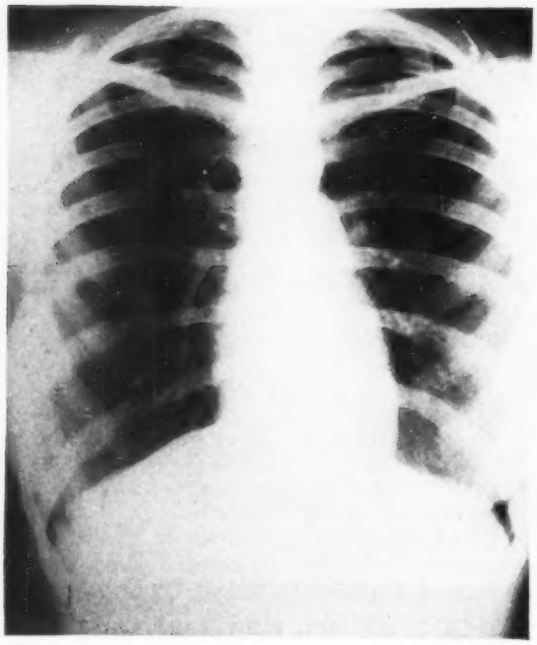

FIG. 1.—July 1949; normal radiograph of chest.

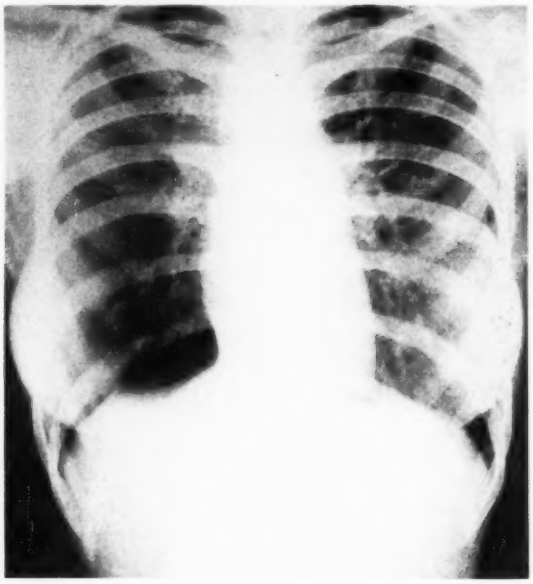

FIG. 2.—December 1952; fine granular opacities evenly distributed throughout both lungs (Category 3, mixed type); cyst in right cardiophrenic angle and elevation of hilar structures.

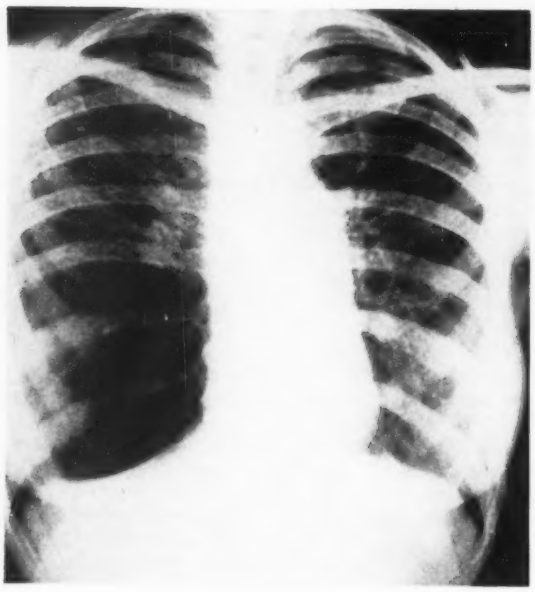

FIG. 3.—March 1953; cyst very much larger.

FIG. 4.—Right middle lobe at thoracotomy showing cyst attached to lower part of lobe (Department of Thoracic Surgery, Shotley Bridge General Hospital).

TABLE 1

SUMMARY OF INVESTIGATIONS

Investigations	1952 December	1953			1954	1955	
		Jan.–Feb.	April	September		January	December
Haemoglobin	102% (15·1 g.%)	108 % (16 g.%)	96% (13·8 g.%)	90% (13·3 g.%)			107% (15·8 g.%)
Red blood cells			4·93 million	5·2 million			
White blood cells		7,400 (normal differential count)	5,700	8,800 (normal differential count)			25,900
Packed cells volume			45%	41%			
Mean corpuscular volume				78·9			
Mean corpuscular haemoglobin				26·4			
M.C.H.C.*				33·6			
Proteins				Albumin 5·2 g.% Globulin 1·8 g.%			
Serum calcium				10·4 mg./100 ml.			
Erythrocyte sedimentation rate	72 mm./hr. (Westergren)	30 mm./hr. Westergren)	23 mm./hr. (Wintrobe corrected)	29 mm./hr. (Westergren)			
Blood group			A. Rhesus + ve; indirect Coombs test negative				
Wassermann Reaction			Negative				
Sputum	Negative for *M. tuberculosis* (including culture)	3 specimens negative (including culture)	8 specimens negative for acid fast bacilli		Negative		
Electrocardiogram				Normal	Right axis deviation (May)	Sinus rhythm; right axis deviation (more marked)	Sinus rhythm; 130/min. R.A.D.: flat diphasic T. wave in left ventricle leads
Tuberculin test	1/100 negative	Negative to 1/100		Negative to 1/100 O.T.			
Cerebrospinal fluid		Normal					
Weight	104½ lb. (normal 116 lb.)	108 lb.	102½ lb.	104 lb.	98 lb. (April)	116 lb.	
Urine							
Albumin	None			None			
Sugar	None			None			
Cells				None			
Beryllium		None in 24-hr. specimen					
Ketosteroids				3·6 mg./24 hrs.			
Liver Function							
Plasma bilirubin				0·1 mg.% directly reacting absent			
Zinc sulphate				6 units			
Thymol turbidity				2 units			
Thymol flocculation				+ + +			
Cephalin cholesterol							
Alkaline phosphatase (Jenner and Kay)				4·9 units			

*Mean cell haemoglobin content.

University of Edinburgh, who found numerous discrete foci in the lung parenchyma consisting of multinucleated giant cells surrounded by lymphocytes. Many of the giant cells contained doubly refractile crystalline material. No purely fibrotic nodules or diffuse fibrosis was seen, and no caseation. He concluded that the pathology was consistent with beryllosis.

Occupational History.—At the age of 17 years the patient had six months training in chemistry and worked as a laboratory assistant in industry until 1948, when, at the age of 23, she became works chemist for about two years to a firm manufacturing fluorescent lamps in County Durham. Zinc oxide (47%), beryllium oxide (3%), manganese carbonate (3%), and powdered silica (47%) were mixed dry, fused into a frit in an electric furnace and, after regrinding, mixed with acetone to form a paint. After leaving this job she did only clerical work and housework.

In October 1949 atmospheric samples were taken in the laboratory and other parts of the factory by the Department for Research in Industrial Medicine of the Medical Research Council. The beryllium was determined spectrographically after wet ashing the

TABLE 2

PULMONARY FUNCTION TESTS

Test	September 1953	May 1954	December 1954
Maximum voluntary ventilation	44 l./min.	54 l./min.	40 l./min.
Arterial blood O_2 saturation at rest	91%	—	91%
" " O_2 after five minute step test	73%	—	—
" " P_{CO_2}	21 mm. Hg	—	41 mm. Hg
Venous admixture (assuming mixed venous saturation)	14%	—	14%
Resting ventilation	7·5 l./min.	—	—
Ventilatory equivalent for oxygen (at rest)	—	33	35
Mechanical properties of lungs			
Functional elastance	—	—	39 cm. H_2O/litre (compliance = 0·0256)
Mean resistance	—	—	15 cm. H_2O/litre/sec.
Work of inspiration	—	—	0·23 kg.m./litre* (elastic work = 83% of total)
Total non-elastic work of inspiration and expiration	—	—	0·127 kg.m./litre*
Active expiration	—	—	0·012 kg.m./litre*

* These figures multiplied by 8 give the work of breathing in kilogram metres per minute.

samples. In the laboratory itself an air sample collected over a period of 75 minutes on one day contained beryllium 2·7 μg. per cu.m. The level in the pulverizer room was 29·6 μg. per cu.m., while in the furnace room 39·1 μg. per cu.m. were recorded.

Radiograph of Lungs.—A radiograph of the lungs taken in August 1953 showed bilateral evenly distributed fine mottling, without tendency to coalesce and with no cysts or areas of emphysema. It was similar in extent to the standard film of Category 3 mixed type of pneumoconiosis (Pneumoconiosis Research Unit, Cardiff). Absence of part of the right sixth rib, filling in of the costophrenic angle, and a small right apical pneumothorax remained after the thoracotomy. There was also a prominent left border to the heart and some elevation of the hila, especially on the right side. Investigations as an in-patient at this time (September 1953) are shown in Table 1.

Tests of pulmonary function were carried out by Dr. G. L. Leathart, as shown in Table 2. The low arterial saturation at rest is consistent with the diagnosis of a destructive lung lesion such as chronic beryllium granuloma. The earliest physiological abnormality in chronic berylliosis is an impediment to the transfer of oxygen across the gas-blood interface of the lung, probably at the alveolar membrane (Wright, 1950), and the fall in saturation during exercise in this patient suggested that this was the case. Estimation of diffusing capacity would therefore have been of value, but could not be made at this time.

Progress.—Between December 1952 and April 1954 the patient lost nearly 7 lb. in weight, but felt fairly well. The chest radiograph showed, in addition to the earlier changes, broadening of the mediastinum and cyst formation in the right upper zone.

In October 1954 she became pregnant, her breathlessness was much improved, and she lost a morning wheeze which had previously troubled her. There was now early finger clubbing and râles were present diffusely in both lungs. In the electrocardiogram right axis deviation, which first appeared in May 1954, was more obvious.

Further physiological investigations of lung function were made (see Table 2). Despite considerable hyperventilation (V_{O_2} = 33 — 35) the arterial P_{CO_2} was normal, suggesting defective distribution of inspired air to those alveoli which were being perfused. Resistance was calculated from records of intraoesophageal pressure and respiratory excursion; elastance is derived from these records, and from a pressure-volume diagram drawn from an oscilloscope. The elastance was measured during normal respiration and is a dynamic or functional elastance rather than a static one. The work done was calculated from the area enclosed by the pressure-volume diagram. In all cases the figure given is the mean of a number of different breaths. Both the elastance and the resistance are greater than normal, and this is reflected in the total work of breathing which is about six times as great as normal. The increased elastance might well be due to fibrosis of the lungs and is much greater than can be accounted for by the lobectomy. The increased resistance suggests obstruction or distortion of the airways, and the blood chemistry supports this.

In January 1955 she had a left spontaneous pneumothorax (Fig. 5). The radiological lung changes were now coarser and the translucent area in the right upper zone was larger.

In May 1955 she had an uneventful delivery of a normal child under the care of the Department of Obstetrics and Gynaecology of Newcastle General Hospital.

She remained fairly well, apart from breathlessness on exertion, until in December 1955, she went into acute right heart failure during a spell of foggy weather and died two days after admission to hospital.

Pathology.—At necropsy there were greatly enlarged mediastinal lymph nodes which showed a reddish oedematous cut surface with here and there some grey speckling. A small calcified focus about 0·2 cm. in diameter was present in the inferior group, but there was no other evidence of tuberculosis. The heart weighed 250 g. and showed dilatation of the right side with hypertrophy of both auricular and ventricular muscles. The left side was normal.

The lungs together weighed 1,600 g. The parenchyma of the right upper lobe was almost entirely replaced by a large smooth-walled cavity about 5 to 6 cm. in diameter, traversed by fibrous cords and communicating with a bronchus to the upper lobe. Smaller cavities, up to 2 cm. in diameter, were also present throughout the upper lobe. The cavities were mainly anterior, while posteriorly the lung tissue was oedematous and contained multiple small firm greyish spots less than 1mm. in diameter, and similar to miliary tubercles. They appeared to be more numerous in the middle lobe and in the upper portion of the lower lobe than in the upper lobe. The left lung was distended with formalin for section later (Fig. 6).

Histology of Lungs.—There are three distinct types of lesion: first, very small collections of epithelioid cells, with or without central necrosis, and usually in relation to a conchoidal body (Fig. 7). These lesions are mainly in the lower lobes in relation to the respiratory bronchioles and are similar in position to the early lesions of tuberculous bronchopneumonia, to which they bear a strong morphological resemblance. One or more Langhans type giant cells may be present, but the giant cell reaction is mostly of the foreign body type, and they contain foreign material which is sometimes doubly refractile (Fig. 8).

The second type of lesion is slightly larger and visible to the naked eye as a pin-head grey nodule. It consists of a central zone of hyaline eosinophilic material without recognizable nuclei, and there are usually several giant cells containing conchoidal bodies at the periphery

FIG. 6.—Sagittal section of left lung showing large central cysts, some of which are dilated bronchi. The small lung lesions are not visible. There is a recent infarct at the lung base.

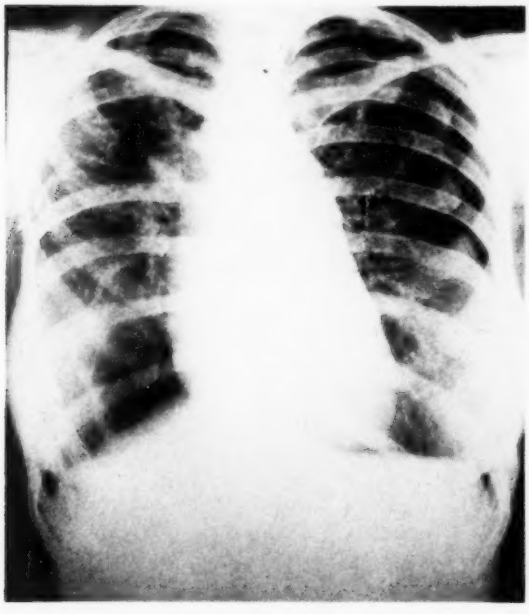

FIG. 5.—January 1955; left pneumothorax and enlarged heart with prominent pulmonary arteries. The lung shadows are now coarser and there is a translucent area in the right upper lobe.

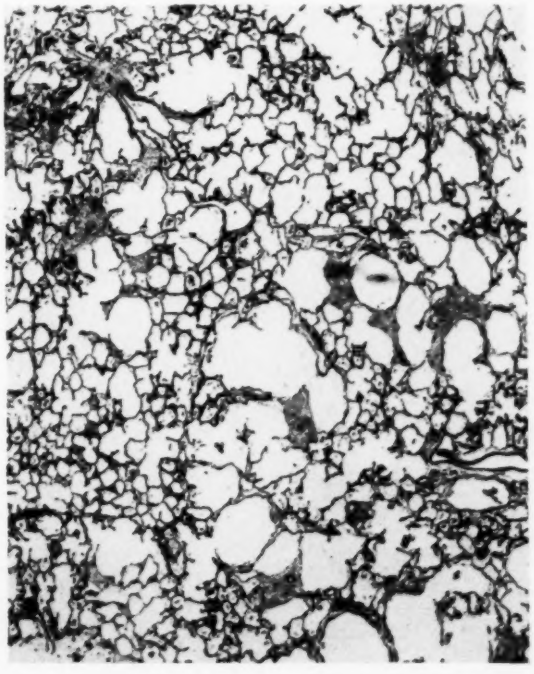

FIG. 7.—Lung showing early lesions with surrounding emphysema. (H. and E. × 23.)

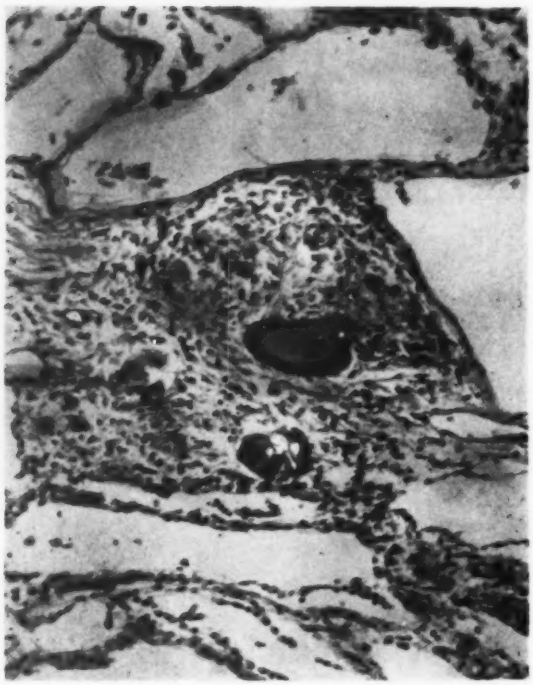

FIG. 8.—Lung; partially crossed polarized light with doubly refractile material in a multinucleated giant cell, surrounded by epithelioid cells. (H. and E. × 100.)

FIG. 9.—Lung; later lesion showing central necrosis, and resembling a caseous tubercle. (H. and E. × 36.)

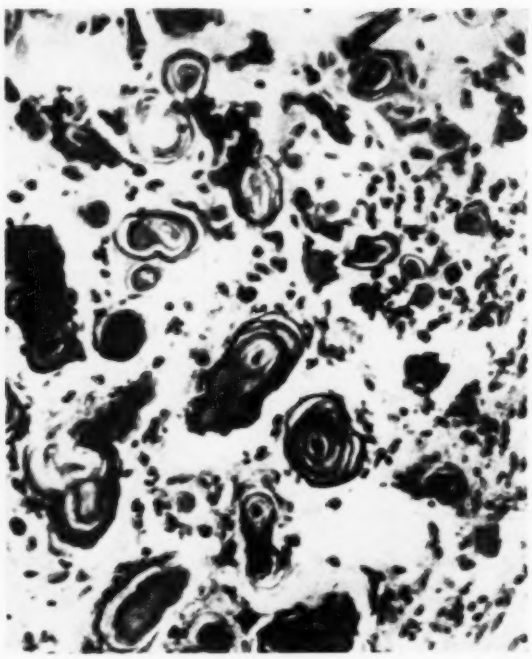

FIG. 10.—Lung; collection of conchoidal bodies in upper lobe cavity. (H. and E. × 270.)

FIG. 11.—Lung; high power view of conchoidal body in an early granuloma. (H. and E. × 375.)

(Fig. 9). The conchoidal bodies show concentric basophilic lamellae surrounding crystalline doubly refractile material (Figs. 10 and 11). This type of lesion is usually surrounded by fibrous tissue, and it greatly resembles inactive or slowly progressive fibrocaseous tuberculosis, or silicosis. The lesion appears to enlarge slowly and may coalesce with neighbouring lesions. It seems probable that they eventually break down and discharge their contents into the bronchi to form the third type of lesion which is a smooth-walled space resembling a chronic tuberculous cavity traversed by cords formed by vessels and bronchi. The walls of these cavities are fibrous and without obvious epithelial lining, and many of them contain large numbers of the conchoidal bodies.

Transitional stages can be traced between the early tubercle-like granulomas and the later pin-head type. The mediastinal lymph nodes contain hard areas of hyaline change similar to that found in silicosis, and there are conchoidal bodies and giant cells as in the lungs.

No tubercle bacilli were found on direct examination or on culture of the tissues. By specific staining methods (Denz, 1949; Pearse, 1957) beryllium was demonstrated in conchoidal bodies in both the lungs and in regional lymph nodes. Dr. A. S. Curry of the North East Forensic Science Laboratory, Harrogate, using arc emission spectrography with a limit of detection of 0·1 μg., reported beryllium in the lung on chemical examination in a concentration of 20 μg. per 100 g. formaldehyde treated wet tissue. A mediastinal lymph gland also contained beryllium in a concentration of 10 μg. per 100 g. tissue.

Some tissues were also analysed by Dr. J. Steel of the Department of Industrial Health, using a method described by Aldridge and Liddell (1948) which is specific for beryllium in biological material except bone, and suitable for quantities greater than 1 μg. The results were as follows:

Lymph node	100 μg./100 g. wet tissue
Lung	40 μg./100 g. wet tissue
Mediastinal gland	6 μg./100 g. wet tissue.

Specimens of tissue from pectoral muscle, liver, kidney, and spleen did not contain any beryllium.

Discussion

In Europe before and during the Second World War acute illness from the use of beryllium in industry was observed and described, together with necropsy findings. Chronic beryllium pneumonitis of delayed onset was first described in America by Hardy and Tabershaw in 1946. In the United States beryllium was used very little until 1938, after which there was rapid expansion of the fluorescent lamp industry, when large numbers of workers handled beryllium phosphors in various proportions.

Manufacture of fluorescent lamps in Great Britain did not begin on a large scale until after 1945, and a smaller amount of beryllium (often only 5%) was used in the phosphors than in the United States (Williams, 1956). In the United Kingdom five out of six workers affected by beryllium pneumonitis were chemists engaged in the development of beryllium lamp powders (McLaughlin, 1955), and of the six reported cases of chronic lung disease four were exposed to the dust of these powders, the remaining two being in contact with 2% beryllium-copper alloy. The particularly hazardous nature of lamp manufacture arose from the mixing and grinding of powder and from cleaning off phosphor deposited on the inside of the glass tubes, all of which produced dust. Ignorance of the deadly nature of the powder which existed in the industry until about 1948 resulted in lack of adequate precautions, even although the use of powdered silica in high proportion by itself suggests the need for stringent precautions.

In our patient the diagnosis of berylliosis was made during life on the combination of typical radiological changes, an occupational history of exposure to a beryllium compound, a lung biopsy showing granulomatous changes, and the characteristic clinical course of the disease. At necropsy confirmation was obtained from the full lung histology and chemical analysis of tissues for beryllium. We have also demonstrated beryllium in lung sections using the dye solochrome azurine which was shown by Pearse (1957) to form an almost black complex with beryllium in neutral or alkaline solution.

The insidious onset with lassitude, loss of weight, breathlessness, and the discovery of bilateral disseminated infiltration in the lungs which was at first confused with miliary tuberculosis and the progressive fibrosis, cyst formation, spontaneous pneumothorax, cor pulmonale, and death from heart failure, are typical of reported cases (Slavin, 1952; Hardy, 1955; Williams, 1956). A diagnostic patch test was not used in view of the reported reaction in a patient to such a test (Sneddon, 1955), when for several days afterwards dyspnoea appeared to get worse and moist râles appeared in the lungs for the first time.

Our view that the histological changes in the lungs and lymph nodes in our patient are characteristic of chronic beryllium granuloma was confirmed by Jones Williams (1958) who included sections of her lung in a review of material from 52 patients with the disease; the great majority were from the United States.

In the present case a prominent feature, of which there are other examples in the literature, was the tendency to cyst formation (Fig. 6). The cavities persisted and enlarged, presumably because of destruction of lung tissue by the granulomatous process, and they interfered with ventilatory function

by increasing the dead space and compressing adjacent lung.

Pregnancy in patients with berylliosis has been recorded, but there are conflicting opinions about its effects on the course of the disease. The effect of pregnancy in our patient appeared to be beneficial, and her symptoms improved so much that treatment with corticotrophin was withheld. After delivery the feeling of well-being was maintained, although she continued to be breathless on exertion.

Enlargement of the adrenal cortex occurs in pregnancy, and Venning (1946) has shown that there is a rise in urinary corticoids to relatively high values. After parturition excretion returns to normal levels again. The subjective improvement during pregnancy which our patient noticed could have been due to the effect of relatively high corticoid production, but the improvement was maintained for about six months after the child was born, during which corticoid output was presumably normal.

In other case reports from the United Kingdom beryllium was not found in the patients' tissues. Wood *et al.* (1958) detected none on chemical analysis of lung and Sneddon (1955) found none in skin. In our patient beryllium was demonstrated in lung sections and its concentration was estimated in portions of lung and lymph gland. In 1949 Denz, using naphthochrome green B, showed that soluble beryllium salts, which readily combine with protein and cause local necrosis, were easily identified by staining. On the other hand, the refractory oxide of beryllium and the silicate which are insoluble in water were not readily stained and did not produce necrosis. Deposits as small as 2 μg. are detectable by this method. In the present case the stain gave positive results with much of the foreign material in the lung. This suggests that insoluble beryllium in the lung may eventually become soluble and combine with protein, and exert a toxic action on the tissue.

Two lesions characteristic of the beryllium lesion are present in material from our patient; inclusion bodies and a series of concentric lines round them (Figs. 10 and 11). Pearse (1957) shows a section of lymph node from our patient stained with solochrome azurine in which there is a crystalline doubly refractile deposit surrounded by a black zone where a soluble beryllium salt is combined with protein. The concentric lines round the deposit are similar to those described by Wood *et al.* (1958) in a section of lung from their patient. In their case there were numerous inclusion bodies both in giant cells and extracellularly, consisting of long refractile needles and conchoidal bodies. The latter had an irregularly shaped central part which was either a deeply stained amorphous mass or colourless plates not refractile to polaroids, with a series of concentric lines, the outer being heavy and the inner ones thinner. These bodies contained calcium and iron. In spite of the long clinical history fibrosis was not a feature of their case.

In our patient the nature and origin of the doubly refractile crystals is obscure. Pearse (1957) appears to assume that the crystalline doubly refractile body shown in the histological section of a lymph node from our patient is beryllium, but produces no evidence in support of this. After incineration the crystals disappear on treatment with acid and are therefore not silica. Whatever their nature they appear to be a product rather than the cause of the reaction, for they are too large to reach the alveoli in the inspired air and appear to be much too large to be carried to the mediastinal glands by lymphatics.

Our patient was exposed to several different substances in the course of her work. During 1949 she handled a mixture containing 3% beryllium oxide in a dry state and 47% powdered silica, at first without any form of protection, although gauze masks were supplied later. She was also exposed to the same materials after they had been fused and ground, and there was therefore not only the possibility of the inhalation of silica and beryllium, but also of the crystalline form of silica, cristobalite, which is seldom found naturally but may be produced by heating silica to high temperatures. It can produce granulomatous changes in the lungs (Vigliani and Mottura, 1948), and is a more fibrogenic substance than quartz though less so than tridymite, another form of silica (Zaidi, King, Harrison, and Nagelschmidt, 1956). Both quartz and cristobalite were detected by *x*-ray diffraction in lung tissues from our patient. In an attempt to identify the individual crystalline particles seen in the lung sections, their refractive indices were measured by Dr. M. H. Battey of the Geology Department, King's College, University of Durham. Extreme values of 1·488 and 1·611 were found, a large proportion of grains examined having an index near 1·488. The grains dissolved in dilute (1:9) hydrochloric acid without effervescence, and we confirmed this. The findings suggested that several different substances were present and that the predominant crystals were not cristobalite or any form of silica, although these might also have been present in the lung; nor were they manganese carbonate or zinc oxide, both of which she handled. In diatomaceous earth pneumoconiosis, which is probably due to inhalation of cristobalite, the lung lesion differs from that found in berylliosis. It is a diffuse granulomatous change

affecting primarily the alveolar walls but extending into alveoli, and later becoming fibrotic. The giant cells are scanty and there are no tubercle-like aggregations (Vigliani and Mottura, 1948).

Jones Williams (1958) points out that the doubly refractile crystals which are present in 80% of conchoidal bodies are not diagnostic of beryllium disease, as they are identical with those found in sarcoidosis, and that conchoidal bodies are also found in tuberculosis, sarcoidosis and silicosis. He believes (1959, personal communication) that the crystals are probably calcite, that the conchoidal bodies are composed of calcium-impregnated protein, and that they are secondary to the crystal formation. Calcite has refractive indices of 1·486 and 1·658 which is consistent with our findings, except that a majority of crystals with the higher index might be expected. Furthermore, we did not observe effervescence with hydrochloric acid which should occur if the crystals were calcium carbonate. In caseation there is deposition of calcium salt usually combined with phosphates. In our patient, although phosphate was probably present as shown by testing with ammonium molybdate, carbonate might well be the main constituent. Why crystals are formed in this way still remains to be explained.

The histological changes in the lungs of this patient strongly suggest a continuous process with lesions of different ages, beginning as microscopic granulomas containing giant cells and foreign material, and progressing to macroscopic nodules with central necrosis and fibrosis. Finally, there is cyst formation by discharge of material containing beryllium-protein complex which can spread throughout already sensitized lung by the bronchi and lymphatics to give new lesions. This mechanism will explain the formation of fresh lesions even after a long period since the initial exposure to beryllium. It is known that beryllium may be retained in the body tissues for up to 10 years (Klemperer, Martin, and Van Riper, 1951), particularly in the lungs.

The analogy with tuberculosis, and perhaps with sarcoidosis, is strong. Assuming that beryllium combines with tissues or plasma protein to form an antigen and that isoimmunity develops, it is possible that if the release of beryllium-protein compound in a soluble or easily available form occurs slowly but continuously, the conchoidal bodies result from a "Liesegang" phenomenon (Van Oss and Hirsch-Ayalon, 1959), in which concentric lines of protein precipitate attract a deposit of calcium and iron. The Liesegang phenomenon occurs in antibody-antigen systems, as seen in gels (Feinberg, 1957), and was originally described in connexion with inorganic salts in porous media or gels (Liesegang, 1896; Van Oss and Hirsch-Ayalon, 1959). This suggests that conchoidal bodies may be formed in very slowly progressive granulomas, and it is interesting that they occur in silicotic lesions but have not been reported in rheumatic nodules. The silicotic nodule may also have an immunological origin (Vigliani, 1958).

The slow liberation of beryllium may also lead to tissue destruction through direct necrosis (Aldridge, Barnes, and Denz, 1949) wherever beryllium is deposited, whether in lung or lymph nodes.

The tendency of beryllium salts to cause dermatitis and the response of patients with berylliosis to patch tests with material containing beryllium salts suggest a sensitivity reaction in certain individuals. The rarity of lung disease amongst those exposed to beryllium (DeNardi, Van Ordstrand, Curtis, and Zielinski, 1953), and the minute quantities which must in some instances have led to the chronic lung disease, also support this.

Sterner and Eisenbud (1951), in a detailed discussion of the possible mode of action of beryllium in the human body, consider that granuloma is one of the histopathological lesions of allergy, and that the essential mechanism in beryllium granuloma is a modified immunological reaction.

Recently, sensitivity has occurred to very small amounts of another rare metal, zirconium, used as sodium zirconium lactate in stick deodorants, with the formation of axillary granulomas composed of epithelioid cells and giant cells surrounded by lymphocytes (Rubin, Slepyan, Weber, and Neuhauser, 1956; Shelley and Hurley, 1958). Sensitivity to beryllium appears to be of quite a different order compared to that of zirconium sensitivity which is not associated with lung lesions, and it presents a very difficult problem in prevention. Because such minute quantities of beryllium can cause profound results, not only must the atmospheric concentration be kept rigidly under control, but individuals known by skin tests to be sensitive to it should not be allowed in the vicinity of processes in which it is being used. Williams (1956) quotes a provisional figure of 2·0 μg. per cu.m. air as the "daily weighted average exposure" below which atmospheric levels should be kept.

In the laboratory in which our patient worked a single estimation of beryllium in air was 2·7 μg. per/cu.m., but in other parts of the factory to which she had access the levels recorded were 10 or 20 times as much and it is likely that her exposure was heavy.

No other case of berylliosis from this factory is

known to us, although a number of men and women were employed on the same process during the relatively short period during which beryllium was in use. The company went into liquidation in March 1950, but in 1953 22 of the former employees were traced and had chest radiographs. Again in 1956 11 former employees were radiographed, two of them for the first time. No gross abnormality was seen in any of the films, but in one man of 59 years who was once a coal-miner for 10 years there were dust opacities of Category 1 or less which had not progressed between 1953 and 1956.

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OBSERVATIONS ON THE PATHOGENESIS OF SILICOSIS BY MEANS OF THE DIFFUSION CHAMBER TECHNIQUE

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An attempt has been made to determine whether the diffusion chamber technique can be used to decide the validity of the silica solubility theory of the pathogenesis of silicosis. Small chambers were constructed from membranes of a pore size which allowed free passage of colloidal silicic acid and tissue fluids but which prevented the entry of host cells and the exit of the larger silica particles. Significant fibrosis failed to develop around chambers containing five different forms of silicon dioxide when inserted subcutaneously and intraperitoneally in rats and rabbits. All five forms of silica were actively fibrogenic when brought into direct contact with peritoneal tissues. However, *in vitro* experiments suggest that colloidal silicic acid, the form which may be involved in silicotic fibrosis, does not escape from the chambers. Thus the biological results obtained by this technique do not necessarily invalidate the silica solubility theory of the pathogenesis of silicosis.

The proximate mechanism by which silicon dioxide induces fibrillogenesis is still undecided. The silica solubility theory of the pathogenesis of silicosis, introduced by Gye and Purdy (1922; 1924) and Gye and Kettle (1922), stimulated numerous investigations, some of which cast doubt on the validity of the theory. Gardner (1934) noted that certain silicates were not so active as quartz although they were more soluble. Later Gardner (1937) summarized the evidence for and against the solubility theory, whilst King, Zaidi, and Nagelschmidt (1956) drew attention to the difficulty of reconciling certain experimental findings with it. Holt and Osborne (1953) and Holt and Went (1960) attempted to modify the solubility theory, whilst Jäger (1954) and Seifert (1954) suggested that silicotic fibrosis may depend on surface properties of silica particles. Marks and Nagelschmidt (1959) considered that cellular injury, induced by ingested silica, was an important step in the fibrotic response.

Several attempts have been made to determine the role of soluble silica in silicosis by the *in vivo* use of capsules or chambers made from porous membranes, intended to separate enclosed silica particles from the cellular tissues outside but to permit the exit from the chamber of soluble silica and the entry of tissue fluids. We have applied this technique to an extended range of dusts and have studied the rate at which soluble silica, liberated from particles, diffuses through the membranes under various conditions. Our results confirm that the fibrotic reaction around dust chambers is no greater than around control chambers, but it seems that the amount of soluble silica liberated from the chambers may be too small to be biologically active.

Diffusion Chamber Studies

Methods

The technique adopted was a slight modification of that devised by Algire, Weaver, and Prehn (1954).

Dusts were enclosed in chambers constructed from thin perspex rings, to each side of which a Membranfilter (type 10, pore size $< 0{\cdot}1\ \mu$) was sealed with thin perspex cement. Control chambers were constructed similarly but contained no dust. Chambers were placed in water and sterilized by heating to 70° C. for one and a half hours on three occasions or by steaming for one hour, after which dust and control chambers contained water. Immediately after sterilization 50 chambers containing various dusts and 25 control chambers were inserted subcutaneously into both flanks and into the peritoneal cavity of 20 rats and five rabbits. The dusts included

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(a) four physical forms of silicon dioxide, namely tridymite, cristobalite, quartz, and vitreous silica (a total of 40 chambers with 50 mg. in each), (b) Aerosil, a dried silica gel (five chambers of 10 mg. each), and (c) anthracite (five chambers of 25 mg. each). The siliceous dusts had a Stokes' diameter of 0·5–2 μ; Aerosil particles were 200–300 Å (Nagelschmidt, personal communication) and may thus be regarded as falling within the size range of colloidal particles (Philbrick, Holmyard, and Palmer, 1949); the anthracite was less than 5 μ in particle size. Animals were killed at intervals of one to 12 months. The observations were mostly histological, but some chambers were tested for permeability or for loss of silica dust.

Results

Control chambers in the subcutaneous tissues were often lightly adherent whereas in the peritoneum more were free from adhesions. Histologically controls from rats and rabbits showed a zone of compact fibrosis (60–120 μ thick), which lay externally to the membrane (60 μ thick) and which became more hyaline with the passage of time. This fibrous layer was easily detached from the membrane, to which a single layer of rather flattened cells tended to adhere. The reaction around *dust chambers* was similar to or occasionally less than that shown by controls and was uninfluenced by the type of dust employed, whether siliceous (including Aerosil) or carbonaceous. Previous experiments (A.G.H.) confirmed that all these siliceous dusts (but not the carbonaceous) were fibrogenic when brought into direct contact with the peritoneum of rats. Occasionally siliceous dust chambers ruptured *in vivo* unintentionally and then an intense fibrotic reaction occurred around them.

Several dust chambers (tridymite, quartz, and Aerosil), which had been used in the animal experiments for a year, were subsequently tested to see how easily carboxyhaemoglobin (COHb) escaped from within, through the dust mass and membrane, to the outside. The membrane sealing one side of the chamber was carefully opened and the lower membrane supported in water held in a Petri dish. A little COHb solution was placed on the surface of the dust mass and the dish covered. In no case did COHb escape through the lower membrane in 24 hours.

The dust (quartz and cristobalite) was removed from two chambers taken out of rats after one year. Repeated chloroform extraction dissolved the perspex and the dust-free membranes were discarded. The dust was then heated to 600° C. for 12 hours and weighed. Silica loss averaged 6 mg., *i.e.* 12% of the original weight. Since control experiments with quartz dust chambers not placed in animals showed an experimental error of approximately 2%, about 10% of the dust was lost *in vivo*, a figure which agrees with that obtained by Pernis, Clerici, and Ghezzi (1958) and by Curran and Rowsell (1958).

Tests of Membrane Permeability

Perspex tubes, of the same diameter as the diffusion chamber rings, were sealed at one end with Membranfilter type 10 membranes and used for two sets of experiments.

1. *The rate at which soluble silica, released from dust suspensions in the tubes, escaped through the membranes.*

One ml. of an aqueous suspension of quartz, tridymite or Aerosil (500 and 1,000 mg./100 ml.) was placed in a tube, the sealed end of which was suspended in 5 ml. water in a small waxed beaker. The apparatus was agitated continuously for one to two days and the concentrations of molybdate reactive (MR) and total silica estimated in the surrounding water by the methods of King, Stacy, Holt, Yates, Deidre, and Pickles (1955) and Paterson and Wheatley (1955). MR silica includes the monomeric and oligomeric forms of silicic acid, whilst the difference between the total and the MR silica gives the concentration of polymerized (colloidal) silicic acid. Permeability of membranes was controlled by using 1 ml. of standard silica solution (10 mg./100 ml.) prepared from sodium silicofluoride. All estimations were performed in duplicate on several occasions and the water used was distilled and silica-free.

Little MR silica (0·1 mg./100 ml. or less) escaped through membranes from quartz or tridymite suspensions of either concentration in one to two days; total and MR silica concentrations did not differ significantly, *i.e.* no colloidal silica was detected. In the case of Aerosil suspension (500 mg./100 ml.) the MR silica concentration outside the tube was 0·5–1·0 mg./100 ml. and the total silica concentration was almost identical. Control experiments showed that MR silica solution readily diffused through the membranes and in one day achieved an average concentration of 1·3 mg./100 ml. outside the tubes, while the internal concentration fell from 10 to an average of 1·8 mg./100 ml.

In an attempt to approach *in vivo* conditions other experiments tested the escape of soluble silica from rabbit serum suspensions of dust (1,000 mg./100 ml.) into rabbit serum. All experimental estimations were read against normal rabbit serum as control and the results represent the increase of dissolved silica over the normal of approximately 0·25 mg./100 ml. serum. The external MR silica concentration was again < 0·1 mg./100 ml. from tridymite suspensions and from Aerosil 2 mg./100 ml., whilst from standard silica solution in serum (10 mg./100 ml.) the external MR silica was < 0·5 mg./100 ml. MR and total silica concentrations did not differ in any particular experiment.

2. *The ability of a protein molecule to penetrate a compact mass of dust and a supporting membrane of the same porosity as that used* in vivo *was visualized by means of COHb.*

The same amounts of quartz, tridymite, and Aerosil

TABLE

Experiment	Medium		Time for COHb Penetration (hrs)			
	Inside Tube	Outside Tube	Control (Dissolved Silica)	Tridymite	Quartz	Aerosil
(a)	Water	Water	1	3	3	27
(b)	Water	1 in 4 serum	1	5	5	24
(c)	Water	Undiluted serum	3	24	24	96
(d)	1 in 4 serum	1 in 4 serum	1	8	8	8
(e)	Undiluted serum	Undiluted serum	24	32	32	48
(f)*	Water	Water	1	5	5	1

*Penetration of COHb from without into the tube.

as were used in the animal experiments were weighed into tubes, which were held vertically in a rack with their membrane-sealed ends enclosed by small glass cups. A fourth tube was set up alongside for use as a control. Several procedures were adopted. (a) Distilled water was added to the dust tubes (1 ml.) and to the cups so that the membranes were well covered. After the dusts had settled for six days, 1 ml. silica solution (see above) was placed in the control tube and its cup filled with water. A similar volume of COHb solution was added to each tube without disturbing the dust and the rate at which COHb diffused into the cups was observed. (b) Because the *in vivo* capsules were surrounded and permeated by protein-containing fluid, an attempt was made to study the influence of serum on diffusion of COHb. Water was added to the tubes and cups as in (a) above. Two days were allowed for the dusts to settle and the content of the cups changed to a 1 in 4 dilution of rabbit serum in water; 1 ml. silica solution was placed in the control tube and its cup filled with 1 in 4 serum. To all four tubes COHb was then added. (c) This experiment resembled (b) except that undiluted rabbit serum was used. (d) The only variation from (b) lay in the replacement of water by 1 in 4 rabbit serum inside and outside the dust tubes from the start. (e) This procedure differed from (d) in the use of undiluted rabbit serum, with which the control silica solution was diluted in equal parts. (f) The time taken by COHb to enter tubes containing compact masses of dust and control tubes from without in aqueous media was also observed.

The results (Table) showed that the much smaller Aerosil particles delayed the escape of COHb in aqueous media, presumably because they were in closer apposition than tridymite and quartz particles. Having percolated through the dust down to the membrane, COHb soon appeared in the surrounding fluid. Obstruction of membrane pores by dust particles thus appears unlikely. Serum (1 in 4) around the tubes made no difference, but when placed in the tubes as well penetration through Aerosil was facilitated, apparently due to the formation of a less compact mass than in water. The appearance of COHb from aqueous suspensions into undiluted serum outside the tubes was considerably delayed. The same result obtained with undiluted serum in and around the tubes in the cases of tridymite and quartz, but in the control COHb was also held back; failure of Aerosil to compact in serum probably explained the quicker penetration by COHb as compared with aqueous suspensions diffusing into undiluted serum. Entry of COHb into the tubes from outside was delayed by tridymite and quartz in water but not by Aerosil, possibly because smaller particles are more easily lifted from the membrane and separated than larger, heavier ones.

Discussion

The first attempt to test the solubility theory of the pathogenesis of silicosis by the use of semi-permeable capsules appears to be that of Kettle (1926), who implanted collodion sacs containing insoluble silicon dioxide subcutaneously in rabbits. The inflammatory reaction which developed around the sacs was similar to that evoked by silica in direct contact with the tissues. Banting (1936), on the other hand, failed to demonstrate silicotic fibrosis around cellophane sacs containing fine quartz dust after insertion into the peritoneal cavity. The pore size of collodion membranes is, however, influenced by the method of preparation, about which Kettle and Banting gave no details, and these early experiments cannot therefore be properly interpreted. The development of dry cellulose membranes with a known pore size greatly improved the reliability of experiments with diffusion chambers (Algire *et al.*, 1954). Pernis *et al.* (1958) used quartz in chambers with a pore size of 0·3–0·5 μ and found that no reaction of silicotic type developed around or inside the chambers after seven months in the subcutaneous tissues of rats. By the same technique and with membranes of $< 0{\cdot}1$ μ pore size, Curran and Rowsell (1958) were unable to demonstrate any difference in the reaction around chambers containing quartz or tridymite and those containing no dust or a non-fibrogenic dust when inserted subcutaneously or intraperitoneally in mice and guinea pigs. The evidence from both these investigations was considered to be opposed to the idea that silicotic fibrosis was mediated by solution of silica particles. The biological findings in the present experiments, using membranes of a pore size $< 0{\cdot}1$ μ and large amounts of dust, confirmed previous observations and further showed that the

physical form of free silica particles had no bearing on the fibrotic response. It must be noted that silica in the form of Aerosil, with a particle size smaller than the pores of the membranes, failed to induce fibrosis.

To produce fibrous tissue a minimum local concentration of quartz particles is required (Schepers, 1958). In cultures of fibrogenic cells from embryonic chicken lung Chvapil and Holečková (1959) observed a pronounced stimulation of collagen formation by silicic acid, but its concentration was critical. Above a particular level of silicic acid collagen production was inhibited, whereas a lower concentration of acid was without effect. Similarly, a low concentration of quartz particles in the culture medium proved ineffective and a high concentration inhibitory to collagen formation. Chvapil and Holečková concluded that silicic acid in appropriate strength stimulated enzymatic activity in cells which participate in collagen synthesis. Knake, Peter, and Müller-Ruchholtz (1959) noted that weak (*i.e.* monomeric or oligomeric) silicic acid had no effect on cultures of rabbit and guinea pig lung and spleen. Below a critical concentration silicic acid exists as low polymers or monomer, whilst above this level the acid consists of higher polymers (Scheel, Fleisher, and Klemperer, 1953; James and Marks, 1956). It may be argued, therefore, that only polymerized silicic acid is concerned in fibrosis, just as toxicity studies incriminate the polymerized form (James and Marks, 1956; Glömme, Holmquist, and Swensson, 1958). If few silica particles exist free in the tissues, little silicic acid will be liberated, its concentration in the tissue fluids will be low, and it will be highly dissociated. On this view fibrosis would not be expected. Previous and present results indicate that a small proportion of silica is in fact lost from diffusion chambers *in vivo*, but this loss occurs over a considerable period of time. It seems likely that, from a large mass of silica enclosed in a diffusion chamber, soluble silica will be released mainly by particles close to the membranes and that only a concentration too low to be fibrogenic may escape into the tissues. The failure of highly polymerized silica, in the form of Aerosil, to cause fibrosis around chambers may also be due to the slow rate at which the colloidal particles escape through the membranes and the consequent rapid dilution in tissue fluids to produce low polymers.

The tests of membrane permeability may be interpreted as supporting this view. MR silica, released from dusts kept in concentrated suspension, escaped through membranes in low concentration and serum did not influence significantly its rate of release, although control experiments with dissolved silica suggested that serum might reduce the rate at which it penetrated the membranes. Scheel *et al.* (1953) found that albumin delayed the rate of solution of quartz. Colloidal silica was not released in detectable amounts from aqueous or serum suspensions, even in the case of Aerosil. The passage of COHb through compact dust masses resting on membranes was delayed in the presence of undiluted serum and, under certain conditions, by the smaller Aerosil particles, whilst COHb solution failed to emerge from within used dust chambers in 24 hours. Moreover, undiluted serum retarded the escape of COHb from silica in solution. It is thus conceivable that dissolved silica may diffuse more slowly from the centre of dust masses in the presence of serum and smaller particles. The evidence does not suggest that membrane pores are obstructed by particles. The results of the two types of experiment used to test membrane permeability are not, however, comparable; escape of MR silica was measured from dust maintained in suspension, but for COHb diffusion studies the dust was tightly packed. The presence *in vivo* of a fibrous layer around the chambers may impede the solution of silica. It must be noted that within the period of the permeability studies free silica induced a vigorous reaction when in direct contact with the peritoneal tissues of rats.

Our biological findings with diffusion chambers resemble those of Pernis *et al.* (1958) and of Curran and Rowsell (1958), but, on the basis of the tests of membrane permeability, we interpret them differently. Pernis *et al.* and Curran and Rowsell considered that the tissue response to silica could not be attributed simply to the continuous application of low or high polymers of silicic acid; but the present results suggest that polymerized (colloidal) silicic acid, the form which is toxic and which may be fibrogenic, does not emerge from the chambers. Although the pores of the membranes we used were theoretically large enough to allow the passage of high polymers of silicic acid (*e.g.* Aerosil), silica particles enclosed in chambers evidently dissolved too slowly and the solution escaped too quickly to achieve the local external concentration necessary for polymerization. Unlike the previous workers, we do not therefore believe that this type of experiment can be used to decide the validity of the silica solubility theory of the pathogenesis of silicosis. To induce fibrosis closer contact is evidently needed between cells and silica than the membranes permit, but dissolved silica in high concentration and hence in a polymerized form may still be involved. This state may be achieved only after phagocytosis of silica particles, though the fact of ingestion, as observed by conventional means,

does not suffice to distinguish between solution and a surface effect as the mechanism by which silica acts.

We are indebted to Dr. G. Nagelschmidt for providing the sized dust samples.

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Brit. J. industr. Med., 1961, **18**, 148.

THE EFFECTS OF VOLE BACILLUS VACCINATION OF AFRICAN MINE WORKERS IN THE NORTHERN RHODESIAN COPPER MINES

BY

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From the Pneumoconiosis Medical and Research Bureau, Kitwe, Northern Rhodesia

(RECEIVED FOR PUBLICATION AUGUST 31, 1960)

African mine workers exposed to siliceous dust in the metalliferous mines of Northern Rhodesia were tuberculin tested; of 17,697 tested, 13,667 were tuberculin positive and 4,030 negative. The negative reactors were divided at random into two approximately equal groups and 1,984 were vaccinated with vole bacillus vaccine and 2,046 were left unvaccinated. These two groups were subsequently followed up and their original radiological categories at the time of tuberculin testing and vaccination were compared with their radiological categories after varying periods of further dust exposure. The object of the investigation was to ascertain whether or not vaccination with vole bacillus vaccine introduced an accelerating factor in the rate of radiological change in pneumoconiosis. The results of the investigation showed that radiological changes in the two groups were minimal and that there was virtually no difference between them. No accelerated changes were recorded in the negative vaccinated group. This is regarded as evidence that anti-tuberculosis vaccine does not introduce an accelerating factor in pneumoconiosis.

No case of pulmonary tuberculosis occurred in the negative vaccinated group. Three cases were recorded in the negative non-vaccinated group, suggesting that vaccination with vole bacillus vaccine affords some measure of protection against tuberculosis, and in view of the absence of any evidence that it had an accelerating effect in pneumoconiosis it appears desirable that miners should receive this protection.

Massive fibrosis is accepted by many as being a modified form of pneumoconiosis, characterized by excessive fibrosis due to the combined action on the lung of a low-grade infection and the specific dust causing the pneumoconiosis. We believe, with other workers in the field of pneumoconiosis, that this infective element is tuberculous (Gough, 1947; Fletcher, 1948; Heppleston, 1951; Cochrane, 1954; James, 1954).

Animal experimental studies especially those of King (1957) and Byers and King (1959) have shown that the intratracheal administration of attenuated tubercle bacilli (vole or B.C.G.) and dust, administered either intratracheally or by inhalation, produces lesions resembling the progressive massive fibrosis seen in industrial workers' pneumoconiosis.

Although there is little similarity between the very large dose of vole bacilli and dust introduced intratracheally into the lungs of animals in these experiments and the very small dose of vole bacilli given intracutaneously in vaccination, nevertheless the advisability of vaccinating workers who have dust fibrosis or who are exposed to that hazard is not universally accepted in view of the theoretical possibility that in so doing a potential accelerating factor may be introduced.

This paper gives an account of the effect of vaccinating with vole bacillus vaccine African mine workers who had been exposed to siliceous dust both before and after vaccination. The vaccination was carried out as an independent research by the Tuberculosis Research Association, Kitwe, under the direction of Dr. Honor Smith and Dr. R. L. Vollum of the Radcliffe Infirmary, Oxford. A full account of this investigation will be published in due course. Its object was to assess the value of vole bacillus vaccine in an African population which included, *inter alia*, African mine workers of four of the major copper mines of Northern Rhodesia

who were subject to the provisions of the Pneumoconiosis Ordinance of Northern Rhodesia implemented by the Pneumoconiosis Medical and Research Bureau.

Brief History of Pneumoconiosis Legislation, the Medical Bureau and the Mines of Northern Rhodesia

Pneumoconiosis legislation in Northern Rhodesia was first enacted in 1945, and established the Pneumoconiosis Medical and Research Bureau. The Bureau, a government institution, is staffed by full-time medical officers and is equipped to carry out all chest and ancillary diagnostic procedures. There is also a fully equipped pathological laboratory and facilities for animal experimental studies. The Pneumoconiosis Ordinance of Northern Rhodesia demands that every European and African mine worker must hold a valid certificate of fitness issued by the Bureau before he is permitted to work in an occupation with a pneumoconiosis hazard. The issue of a certificate for engagement (initial certificate) is dependent upon the prospective employee passing a clinical examination and a radiological examination of his chest on a full-size film. Thereafter he must attend at yearly intervals for further examination (periodical certificate) at which a further clinical and radiological examination on a full-size film is carried out. On leaving mining he is finally clinically and radiologically examined (discharge examination). The average number of mine workers examined each year is 5,000 Europeans and 35,000 Africans.

Small deposits of copper oxide ore have been mined intermittently in Northern Rhodesia since 1910. Large deposits of sulphide ore were known to exist, but it was not until the flotation process was developed that they could be worked profitably. When this process was perfected, large-scale development began in 1926 and the first production took place in 1929. From this beginning six major mines have been developed which produced more than 500,000 tons of copper in 1959, making Northern Rhodesia the second largest copper producing country in the world.

Dust sampling on these mines is the joint responsibility of the Government Mines Department and the ventilation departments of each mine. The Mines Department uses thermal precipitators and Hexhlet apparatus and the ventilation departments of the mines employ the Rand Konimeter for " snap sampling ". The agreed maximum permissible limit of dust particles between 0·4 and 7·0 μ is 350 per ml., but in fact counts in most operations are lower than this. The free silica content of this fine atmospheric dust is determined by the *x*-ray diffraction method using the Geiger counter technique; the average free silica content of the atmospheric dust in the above range in the four mines taking part in this investigation is Mine A: 43%; Mine B: 28%; Mine C: 23% and Mine D: 19%. African mine workers from these four mines constitute the population on which our observations have been made.

Tuberculin Testing and Vaccination

Purified protein derivative (P.P.D.) in a concentration of 2 mg. per ml. was used in the tuberculin testing. This was obtained from the Veterinary Laboratory of the Ministry of Agriculture and Fisheries, Weybridge, Surrey. One minim of 1/100 adrenalin was added to 1 ml. of P.P.D. and the tuberculin was applied to the cleansed skin of the flexor aspect of the forearm by means of a glass rod. The tuberculin test was made with East's modification of the Heaf multiple puncture apparatus set at a penetrating depth of 2 mm. The reaction was read 72 hours later. The negative reactors were divided at random into two approximately equal groups, one receiving the vaccine and the other remaining unvaccinated.

The programme of testing was as follows: Mine A, January to February 1956; Mine B, September to October 1954; Mine C, April to July 1954; Mine D (this constituted the largest number, therefore tuberculin testing was spread over two main periods): D1, November 1952 to January 1953; D2, December 1954 to February 1955. Vole bacillus vaccine was administered by means of a Birkhaug multiple puncture machine (40 needles) set at a penetrating depth of 2 mm.; the site of inoculation was the left upper arm above the deltoid insertion. Vaccination was carried out immediately after tuberculin testing and took place during the same periods as specified in the tuberculin testing programme.

Radiological Classification

The radiological classification used to describe the classical silicosis encountered in the copper mines of Northern Rhodesia and used to describe the radiological changes in this investigation is as follows:

" O " (Normal). Normal thorax.

" I " (Indeterminate). In this category there is a general increase in the lung marking of indeterminate cause.

" L " (Linear). This category is characterized by the presence of numerous fine linear lung markings usually tending to obscure the normal pulmonary vascular pattern and sometimes associated with enlargement of the hilar glands.

" N " (Nodular). This category is characterized by the presence of nodular opacities and is subdivided into three depending on the size and profusion of the nodules.

TABLE 1

SUMMARY OF RESULTS, WITH CHANGES IN RADIOLOGICAL CATEGORY

Mine and Period Surveyed	No. at Time of Tuberculin Testing	Tuberculin Reaction	Radiological Category at Examination Nearest to Time of Tuberculin Testing	Average Age at Time of Tuberculin Testing (yrs)	Average Dust Exposure at Time of Tuberculin Testing (mths)	Subsequent Dust Exposure (mths)	Radiological Changes Occurring From Time of Tuberculin Testing Until 1958			
							L	N	MF	TB
A 1956/58	2,296	Positive	O	36	85	17	16	—	—	6
	166	Positive	L	43	160	19	—	10	—	7
	43	Positive	N	48	200	17	—	—	4	1
	10	Positive	MF	44	186	15	—	—	—	2
	247	Negative; vaccinated	O	32	66	16	—	—	—	—
	8	Negative; vaccinated	L	39	128	14	—	—	—	—
	212	Negative; not vaccinated	O	32	70	17	1	—	—	2
	4	Negative; not vaccinated	L	40	120	21	—	—	—	—
	1	Negative; not vaccinated	N	40	210	24	—	—	—	—
B 1954/58	1,673	Positive	O	32	63	27	30	1	—	4*
	42	Positive	L	41	119	31	—	3	—	1
	11	Positive	N	47	183	43	—	—	1	—
	2	Positive	MF	50	209	17	—	—	—	—
	189	Negative; vaccinated	O	29	47	26	1	—	—	—
	1	Negative; vaccinated	L	40	150	48	—	1	—	—
	111	Negative; not vaccinated	O	28	44	25	1	—	—	—
C 1954/58	2,760	Positive	O	34	74	32	77	—	—	10*
	87	Positive	L	44	159	35	—	14	1	—
	14	Positive	N	46	189	30	—	—	—	—
	4	Positive	MF	43	150	27	—	—	—	—
	480	Negative; vaccinated	O	32	58	32	9	—	—	—
	4	Negative; vaccinated	L	43	150	33	—	—	—	—
	3	Negative; vaccinated	N	55	270	24	—	—	—	—
	314	Negative; not vaccinated	O	31	56	31	6	—	—	1
	4	Negative; not vaccinated	L	48	195	24	—	—	—	—
	1	Negative; not vaccinated	N	50	210	0	—	—	—	—
D (1) 1954/58	2,256	Positive	O	27	34	12	8	—	—	2*
	11	Positive	L	37	79	10	—	—	—	1
	1	Positive	N	50	210	36	—	—	—	—
	309	Negative; vaccinated	O	26	32	12	—	—	—	—
	593	Negative; not vaccinated	O	25	31	9	—	—	—	—
	1	Negative; not vaccinated	L	40	30	0	—	—	—	—
D (2) 1953/58	4,253	Positive	O	28	49	28	118	—	—	5*
	33	Positive	L	42	157	53	—	13	1	—
	5	Positive	N	46	174	34	—	—	—	—
	738	Negative; vaccinated	O	25	40	25	8	—	—	—
	5	Negative; vaccinated	L	38	105	50	—	1	—	—
	802	Negative; not vaccinated	O	25	40	24	15	—	—	—
	3	Negative; not vaccinated	L	43	150	44	—	1	—	—

* Includes one pleural effusion (positive culture).

"IN" (Infective nodular). In this category the nodules are characterized by their irregular outline, variation in size and density and their tendency to coalesce. It is similarly sub-divided depending on the size and profusion of the nodules.

"MF" (Massive Fibrosis). This category is characterized by the presence of dense fibrosis which is usually non-homogeneous and which has an irregular outline. It is also sub-divided into three according to the extent of the lung fields occupied by the dense fibrosis.

"ST" (Silico-tuberculosis). In this category overt tuberculosis has been superimposed on a background of dust fibrosis.

"TB" (Tuberculosis). Simple pulmonary tuberculosis.

Investigation

In all, 17,697 mine workers took part in the investigation and were tuberculin tested. 13,667 were found to be tuberculin positive, and 4,030 tuberculin negative. The latter were divided at random into two approximately equal groups of whom 1,984 were vaccinated and 2,046 remained unvaccinated. The three groups were analysed at the end of 1958 for any radiological changes that had occurred from the time of original tuberculin testing and vaccination. The radiological examination done at the Bureau nearest to the time of tuberculin testing was recorded in each case and the radiological category at that time was compared with that of subsequent radiological examinations and, finally, with the examination nearest to December 31, 1958.

The films were classified with a knowledge of their dates, but without knowledge of the tuberculin sensitivity of the miner, or whether he had or had not been vaccinated.

Results

The radiological changes are summarized in Table 1.

Discussion

It was not possible to follow up all the mine workers from each mine for the same period of time due to the fact that a proportion of them had left the mines during the follow-up period and were not available for final examination in 1958. Table 2 shows the number of mine workers originally participating in the investigation and the percentage who were finally examined in 1958.

These percentages, it will be seen, vary between the mines and to a very much lesser degree between the three groups of positive, negative vaccinated, and negative not-vaccinated at each mine. The reason for this is to be found in the rate at which African mine workers leave the industry. In a previous investigation (Paul, 1959) it was found that approximately 60% of all new African entrants to the industry left within the first two years. This rapid rate of leaving declines after the first few years of mining service. Mine D had an abnormally large number of these new entrants compared with the other mines, and had a greater discharge rate. The fact that only a percentage of each group was followed up until the end of 1958 may have introduced a bias. But this is considered unlikely in that at each mine both negative groups had approximately the same percentage of miners examined in 1958, and this would imply that the men of the vaccinated and not-vaccinated groups, who left in the intervening years, did so for similar reasons. Analysis of the radiographs of those who did leave in the intervening years shows that all did so with an unchanged radiological category, and from this it is deduced that the reasons for leaving were the customary ones, *e.g.* unsuitability for and lack of adaptability to underground conditions.

TABLE 2

NUMBERS OF MINE WORKERS PARTICIPATING AND PERCENTAGES EXAMINED IN 1958

Mine and Year of Original Testing	Number of Original Mine Workers and (in brackets) the Percentage Examined in 1958		
	Positive	Negative: Vaccinated	Negative: Not Vaccinated
A 1956	2,515 (76%)	255 (75%)	217 (80%)
B 1954	1,728 (52%)	190 (56%)	111 (55%)
C 1954	2,865 (65%)	487 (63%)	319 (63%)
D1 1954	2,268 (21%)	309 (18%)	594 (19%)
D2 1953	4,291 (35%)	743 (31%)	805 (28%)

Reference to the Tables shows that the major radiological changes took place in the tuberculin positive group. This is to be expected as this group consisted of older mine workers who, consequently, had had considerably more dust exposure than those in the two negative groups. The primary concern of the investigation was, however, a comparison between the two negative groups, and it will be seen that the radiological changes recorded in both groups were minimal and that there was virtually no difference between them. None in either negative group developed massive fibrosis or the infective type of nodulation, and there were no accelerated radiological changes recorded in the negative vaccinated group. These findings are regarded as evidence that vaccination with vole bacillus vaccine had no accelerating influence on pneumoconiosis. Further, the three cases of pulmonary tuberculosis recorded in the negative reactors all occurred in the negative non-vaccinated group and, although the number is small, it suggests that the vaccine gave some measure of protection against pulmonary tuberculosis.

Conclusion

In view of the absence of any evidence that vole bacillus vaccine has an accelerating influence in pneumoconiosis, and because of the apparent protective value it has against tuberculosis, it appears desirable that it or other protective anti-

tuberculosis vaccine should be given to tuberculin negative reactors entering an industry with a pneumoconiosis hazard.

I am indebted to Dr. Honor Smith and Dr. R. L. Vollum of the Radcliffe Infirmary, Oxford. I also wish to thank Mr. G. Addison, B.Sc. (Econ.), Statistician to the Bureau, for his assistance.

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THE JANUARY (1961) ISSUE

The January (1961) issue contains the following papers:—

Background to Byssinosis in Ulster. By James A. Smiley.

Pulmonary Fibrosis in Workers Exposed to Finely Powered Aluminium. By John Mitchell, G. B. Manning, M. Molyneux, and Ronald E. Lane.

Pulmonary Fibrosis in a Worker Using an Aluminium Powder. By J. Warren Jordan.

Bronchitis—Sickness Absence in London Transport. By C. J. Cornwall and P. A. B. Raffle.

The Causes of Death in Iron and Steel Workers (Non-foundry). By A. I. G. McLaughlin and H. E. Harding.

A Study of Aspergillus Spores in the Atmosphere of a Modern Mill. By F. C. Stallybrass.

Christmas Disease and Coal-mining. By C. B. Kerr.

Methyl Bromide Poisoning. By E. M. Rathus and P. J. Landy.

Coproporphyrinuria in Groups of Workers as an Index of Inorganic Lead Absorption. By R. L. Zielhuis

Erosion of the Teeth Due to Sulphuric Acid in the Battery Industry. By D. Malcolm and E. Paul.

Observations on the Urinary Protein of Men Exposed to Cadmium Dust and Fume. By J. C. Smith, Agnes R. Wells, and J. E. Kench.

Miscellanea

Book Reviews

A number of copies are still available and may be obtained from the Publishing Manager, British Medical Association, Tavistock Square, W.C.1, price 17*s.* 6*d.*

Brit. J. industr. Med., 1961, **18**, 153.

CEREBRAL TUMOUR IN A LEAD WORKER

BY

R. W. PORTAL

From the Central Middlesex Hospital

(RECEIVED FOR PUBLICATION AUGUST 30, 1960)

A case is reported in which a frontal astrocytoma occurring in a lead worker was initially misdiagnosed as lead encephalopathy. The evidence in favour of lead poisoning as a secondary diagnosis is discussed and details given of the urinary lead excretion in response to intravenous EDTA. It was concluded that though excess lead absorption had occurred, the history and findings were not such as to have made a diagnosis of lead encephalopathy tenable.

Industrial lead poisoning is becoming an uncommon event in this country and instances of lead encephalopathy are now very rare (Hunter, 1957). Many physicians therefore have scanty experience in diagnosing and investigating such cases, which tend to gravitate more and more to centres specializing in industrial diseases. They may not be familiar with the degree of exposure liable to lead to a dangerous level of lead absorption and may have difficulty in interpreting tests which suggest that absorption has occurred. This case is reported not in the hope that it will add anything of value to the literature of lead poisoning, but because it contains certain errors and misapprehensions which it is salutary to put on record. A mistake in diagnosis was made, and it may be of interest to recount the events as they occurred and then review them in the light of the more experienced advice later received.

Case History

A 63-year-old bullion refiner was admitted to hospital on January 1, 1960. He had been in good health up to the night of his admission and had experienced no metallic taste in his mouth, no constipation or colic, and no weakness of the limbs; his wife had observed nothing abnormal in his mental state. On December 31, 1959, at about 11.0 p.m. she found him unconscious in front of the television set. His limbs were stiff, his breathing heavy, and she was unable to rouse him. On arrival in hospital an hour later he was stuporose, irritable and incapable of speech. His left pupil was larger than his right, he did not move his left arm and his left plantar response was equivocal. There was no papilloedema. His blood pressure was 200/100 mm. Hg (160/80 mm. Hg two weeks later). The only other abnormal finding was a profuse crop of very small petechiae on the trunk and limbs which faded in the next day or two. He was edentulous. A lumbar puncture on admission produced clear cerebrospinal fluid (C.S.F.) containing protein 20 mg./100 ml., white blood cells 2/c.mm. and red blood cells 9/c.mm. The cerebrospinal fluid Wassermann reaction was negative. He was too restless for a pressure reading to be taken.

By the following morning he was rational but amnesic for the period since the onset of the attack. All abnormal neurological signs had disappeared. During the next five days he had two more epileptiform attacks in which a transient left-sided weakness was noted. Between these he was at times confused. He was febrile from the second to the fifth day with a maximum temperature of 100·5° F.

It was intended to investigate him routinely as a case of symptomatic epilepsy, but in view of his extensive petechiae a blood film was examined. This unexpectedly showed very coarse punctate basophilia with a stippled red cell count ranging from 6,000 to 12,000 per million red cells. His haemoglobin was 97% and white blood cells 9,000/c.mm.; the platelets were reported as atypical. Chest radiograph, electrocardiogram, skull radiograph and electroencephalogram (E.E.G.) were normal. There was a slight proteinuria, the urine deposit containing epithelial cells only. Blood urea was 46 mg./100 ml. and 29 mg./100 ml. six days later.

On questioning him about his occupation the following facts emerged. On leaving school he had served in the Navy as a signalman for seven years till 1920. He then worked for five years as a fitter in a company producing white lead, but he denied any contact with lead during this period. Since 1925 he had been employed by a London company refining precious metals and except for the war years had worked in the furnace rooms, where for the past few years he had been a charge-hand. Lead is regularly used in the refining process and the employees take precautions to minimize exposure. He thus wore a Martindale mask consisting of a wire frame with a muslin filter. He was normally conscientious about this, though he admits that he sometimes removed it for a smoke.

TABLE 1

Date (1960)	Amount of EDTA Infused (g.)	24-hour Urinary Excretion of Lead (mg.)	Concentration of Lead in Urine (mg./l.)
Jan 4	1	3·78	1·18
Jan 5	—	0·38	0·42
Jan 7	1	2·75	1·25
Jan 8	2	2·88	1·10
Feb 18	—	0·036	0·02
Feb 19	2	2·22	1·0
Feb 20	2	1·45	0·72

On December 22 and 23 (a week before the onset of symptoms), and again on December 28, he was one of a number of men given the special task of transferring by shovel some 12 tons of litharge (PbO) from bins into steel drums. This material consisted of greyish-yellow lumps and powder, the moving of which inevitably raised a certain amount of dust. At the time of this operation he was suffering from a head cold; he was also a heavy smoker who rolled his own cigarettes. He suffered no ill effects, however, while carrying out the work. The employees' urine is tested at intervals for porphyrins, and on looking up the patient's record it was found that the tests had been positive for some time past.

His history of exposure to lead and the coarse stippling of his red cells suggested that his symptoms were due to lead poisoning and that we were dealing with a case of lead encephalopathy. Owing to the three days' delay in diagnosis and the recurrence of fits it was decided to start treatment without undertaking a preliminary control estimation of urinary lead excretion and without pursuing further investigations such as cerebral angiography. On January 4, therefore, an intravenous infusion of 1 g. ethylenediamine tetra-acetate (EDTA, disodium calcium versenate) was administered in 500 ml. of dextrose solution. A 24-hour urine collection started synchronously with the infusion contained a total of 3·78 mg. of lead in 3,200 ml. of urine. The amount of lead in the blood 18 hours after the infusion was 190 mg./100 ml. The ensuing 24-hour excretion of lead (when no EDTA was given) was 0·38 mg. On January 7 a further gramme of EDTA was infused, and three more doses of 2 g. followed in the next four days. The urinary lead outputs on January 7 and 8 were 2·75 mg. and 2·88 mg. respectively. A further course of EDTA totalling 9 g. was given in five daily infusions from January 18 to 23, but lead excretion was not measured. The patient was discharged in apparent good health 23 days after admission.

When readmitted on February 18 for further excretion studies his resting 24-hour urinary lead output was 0·036 mg.; three more daily infusions of EDTA were given, which on the first two days resulted in a rise of lead excretion to 2·22 mg. and 1·45 mg. The results of the various estimations are set out in Table 1.

We assumed at this point that the tissue lead concentration had been reduced to a safe level and no further treatment with EDTA was given. The patient's last fit had occurred on January 6, a week after the onset of symptoms, and his mental state had become normal the next day. He appeared perfectly well and was already back at work where his employment had been changed to avoid any further exposure to lead.

Early in April a message was received from his factory indicating that all was not well. He had been complaining of headache, had unaccountably put on over a stone in weight, and his workmates had noticed that he had lost his usual cheerfulness and was becoming slow and unreliable. Indeed his behaviour during the preceding few days had been so unlike him that he was considered unfit for work. He was readmitted on April 16.

It did not take long to make a diagnosis: reinvestigation showed that he was suffering from a cerebral tumour. The personality change was obvious; he was rational and orientated but ponderous and apathetic. He had a partial left facial palsy and hemiparesis. His C.S.F. now contained 140 mg. of protein at a pressure of 250 mm.; the E.E.G. had become abnormal and indicated a space-occupying lesion in the right fronto-temporal area. Finally carotid angiography (not carried out on his original admission) revealed pathological vessels in the right frontal region with displacement of the right anterior cerebral artery to the left.

He declined rapidly and died four weeks after admission (five months after the convulsion which was his first symptom). At necropsy a large irregular primary tumour with a necrotic centre was found in the right frontal lobe, extending backwards into the parietal lobe. There was no other macroscopic abnormality in the brain and other organs were normal. Histologically the tumour was a fibrillary astrocytoma. Routine preparations from the rest of the brain showed no evidence of nerve cell damage. Microscopy of the kidneys, which to the naked eye were normal, revealed some tubular damage, with variability of the nuclei of the epithelial cells, some cytoplasmic degeneration, and an occasional mitotic figure indicative of regeneration. The damage thus displayed was by no means specific but could be attributed to lead poisoning. The bone structure of femur and vertebrae was normal. Estimations of the lead content of various tissues are given in Table 2.

TABLE 2

LEAD CONTENT OF TISSUES

Tissue	Lead (wet) (μg./g.)
Skull	170
Femur	120
Kidney	
Medulla	2·0
Cortex	2·9
Heart	0·4

Discussion

The patient was at first notified to the Inspector of Factories as a case of industrial lead poisoning. The most significant fact in his history was the recent shovelling of litharge. This is well known among lead workers to be a dangerous substance, and the Martindale mask which he was wearing

could be considered inadequate protection for the task. The sudden increase in absorbed lead resulting from these three days' unduly heavy exposure was presumed to be the final insult superimposed on a background of slow chronic absorption. The work was heavier than he was accustomed to, and the increased pulmonary ventilation involved was well calculated to give ingress to a fine dusty form of a soluble lead oxide. He was in addition a heavy smoker who rolled his cigarettes; inhalation of lead transferred from his fingers to the tobacco was another possible source of undue absorption. He was furthermore suffering from a cold at the time, and intercurrent infections are recognized as enhancing the toxic effects of lead. That his body lead content was already raised was indicated by the positive urinary porphyrin tests recorded in the factory. The high output of lead in the urine in response to EDTA (maximum 3·78 mg./24 hrs; normal 0·22–0·65 mg.) again suggested lead poisoning as a possible diagnosis. Still more support was lent by his immediate improvement after treatment with EDTA, as judged by the disappearance of mental confusion and the cessation of fits.

Despite its rarity in adults lead encephalopathy remains a condition to bear in mind when neurological symptoms develop in a person known to have been exposed to lead. Clinically it may present in a wide variety of ways. Danaraj (1956), for example, reported four cases presenting initially as encephalitis, dementia paralytica (GPI), coma, and an obscure neurological disorder. Three of of these were adults and one a boy of 11; all of them had a raised C.S.F. protein, three had an excess of lymphocytes in the C.S.F. and three had a raised C.S.F. pressure. Akelaitis (1941) emphasized that the clinical picture was that of any severe intoxication of the brain, with its resulting delirium or convulsions. The predominant pathological change was oedema of the brain, probably resulting from vascular damage; exudate was seen in the perivascular spaces, the meninges were oedematous and thickened, and proliferative changes were found in the endothelial cells of the small blood vessels (Akelaitis, 1941; Blackman, 1937).

There have been many accounts of the use of EDTA in lead poisoning since Bessman, Ried, and Rubin (1952) first employed it successfully on a 3-year-old boy with lead encephalopathy. Treatment in the present case was carried out on the lines indicated by Leckie and Tompsett (1958) who undertook investigations on eight wire mill workers, seven of whom had been exposed to lead. They found that increasing the dose of EDTA above 2 g. did not significantly raise the urinary lead excretion, and that the duration of the infusion was of importance in achieving a good output. They suggested an infusion period of six hours, or continuous slow infusion over 48 hours in severe cases. Excessive absorption of lead was indicated by a 24-hour lead output of more than 1·5 mg. in response to 2 g. of EDTA; in control subjects the excretion lay between 0·22 and 0·65 mg. (compare 3·78 mg./24 hours in the present patient). A fall in excretion below 1·5 mg. in the second 24 hours of any course of infusions suggested that the available lead stores were becoming depleted.

The lead content of the patient's bones was at the upper limit of the range found in normal subjects without undue exposure to lead, and probably well beyond it. Estimates for long bones vary from less than 3·8 μg. per gramme wet tissue to 108 μg. (Cumings, 1959). The patient's levels furthermore compare well with values found in known sufferers from lead encephalopathy in whom long bone concentrations ranging from 8·5 to 176μg. per gramme wet tissue have been reported (*Cf.* Cumings). This patient moreover had received three courses of EDTA and it can be assumed that the untreated level would have been higher.

When the cerebral neoplasm was discovered the notification of industrial lead poisoning was withdrawn. In discussing the case later this retraction was criticized on the grounds that the man had after all suffered excess lead absorption as shown by the coarse red cell stippling, high urinary lead excretion and the raised bone lead content, and that his original fit might have been triggered off by a sudden increase of lead in brain or blood. According to this view he might have stood to claim under the Industrial Injuries Acts. The cancellation was defended, on the other hand, by pointing out that the entire clinical picture could be explained by the tumour alone, and that this, in any case, was what killed him. One could not assert that the clinical course would have been any different had there been no exposure to lead at all.

There are indeed certain facts which weigh against the diagnosis of lead encephalopathy and which, had we been more familiar with the subject, would have dissuaded us from postulating this as the cause of the man's symptoms. Though he had worked for 35 years in contact with lead, he was engaged in a process in which the lead hazard was not a serious one. He was therefore, a 'salted' worker, who had not hitherto proved himself susceptible to lead poisoning. The fact that his urinary porphyrin tests were positive is not evidence of a dangerous level of lead absorption. Raised coproporphyrin figures are usual in lead workers and in the absence of quantitative tests a positive

result is of no great value in determining the degree of absorption in any given case. His good health up to the time of the fit, the absence of any symptoms attributable to chronic lead absorption, and in particular his haemoglobin of 97%, should have cautioned us against too ready a diagnosis of lead intoxication, especially its rare manifestation of encephalopathy. A raised punctate count is seen in many lead workers and was particularly likely to occur in someone recently exposed to the lead oxide of litharge dust. It was the coarseness of the stippling, coupled with what was interpreted as a significant history of exposure, that first led to the pursuit of a red herring and the diagnosis of a rare condition rather than a commoner and more probable one. The conclusion is that though excess absorption had occurred the patient was not suffering from lead poisoning, and all his symptoms were attributable to the neoplasm.

Finally, it is of interest to recall that lead compounds have been used with some enthusiasm as cytotoxic agents in cancer therapy. Professor Blair Bell (1930), the Liverpool gynaecologist, undertook the treatment of a wide variety of malignant neoplasms on a considerable scale (566 patients between 1920 and 1928), and claimed successful results in 21% of those who were thought to have had adequate treatment. Organic lead salts were given intravenously at weekly intervals, each injection containing some 25 mg. lead. Primary cerebral growths, however, were not among those recorded as receiving this treatment. One can only speculate whether an increased concentration of lead in the brain would render a patient with a coexisting neoplasm more liable to epilepsy; but in view of the known cytotoxic properties of lead it would be most unlikely to accelerate the growth of the tumour.

The lead estimations were kindly undertaken by Dr. Donald Hunter and Dr. George Kazantzis in the Department for Research in Industrial Medicine, the London Hospital. (Method employed: HNO_3 — $HC10_4$ ashing; dithizone; monocolour.)

I thank Dr. Richard Asher for permission to publish this report, and Professor R. E. Lane and Dr. T. O. Garland for their very valuable guidance and criticisms.

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MISCELLANEA

Preliminary Communication: A Physiological Study of the Effects of Vibration on the Fingers

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(RECEIVED FOR PUBLICATION FEBRUARY 19, 1960)

It has been well known for many years that the long-continued use of certain vibrating tools may lead to the development of Raynaud's phenomenon. Much is known about the clinical aspects of vibratory Raynaud's phenomenon (see, for example, Agate, 1949), but it is not known how the vibration causes this disability. An important study was undertaken by Guillemin and Wechsberg (1953), who found that, after 1,000 hours' exposure to vibration, the rewarming time of albino rats exceeded the normal value.

In our experiments the physiological effect of a short exposure to mechanical vibration was measured on the forefinger. As a physiological test, the Lewis reaction (cold dilatation) was chosen. This reaction, according to Magos and Okos (1955; 1956) is diminished or abolished in patients suffering from Raynaud's phenomenon.

Method

Nine men giving identical results in the cold dilatation test on both index fingers were selected. Six of them (20, 25, 30, 34, 36, and 53 years of age) showed no disorder of peripheral circulation, and three (27, 33, and 42 years of age) suffered from vibratory Raynaud's phenomenon.

Calorimetric examination by Greenfield and Shepherd's (1950) method was undertaken. The distal 2·8 cm. of the index finger was placed in water in the calorimeter at 9·5° C. for 15 minutes. In every experiment at least four calorimetric measurements were made, two of them the day before the vibratory procedure, one after the vibration was applied to the exposed finger, and one on the opposite (control) finger.

The vibratory exposure was made with a plate vibrated vertically by an eccentric wheel at 3,000 cycles per minute with an amplitude of 2 mm. The subjects placed the palmar surface of the terminal phalanx of one index finger on this plate for 10 minutes. After this vibration the subjects immersed both hands completely in a water bath at 25° C. for 10 minutes. The water bath immersion was immediately followed by calorimetric examination. In the experiment undertaken on the day before vibration the calorimetric examination was also preceded by immersion of the hands in a water bath at 25° C. Six subjects (three healthy and three suffering from vibratory Raynaud's phenomenon) were examined in this experiment once, two subjects twice, and one three times.

In the second experimental series the application of vibration was followed by a rest of five minutes. The index finger was then immersed in the calorimeter without previous immersion in the water bath. The circulation of the vibrated finger and of the control finger was arrested by a rubber ring during the first six minutes of the calorimetric examination. In this experiment two subjects were examined once and one three times; all three were from the group without circulatory disorders.

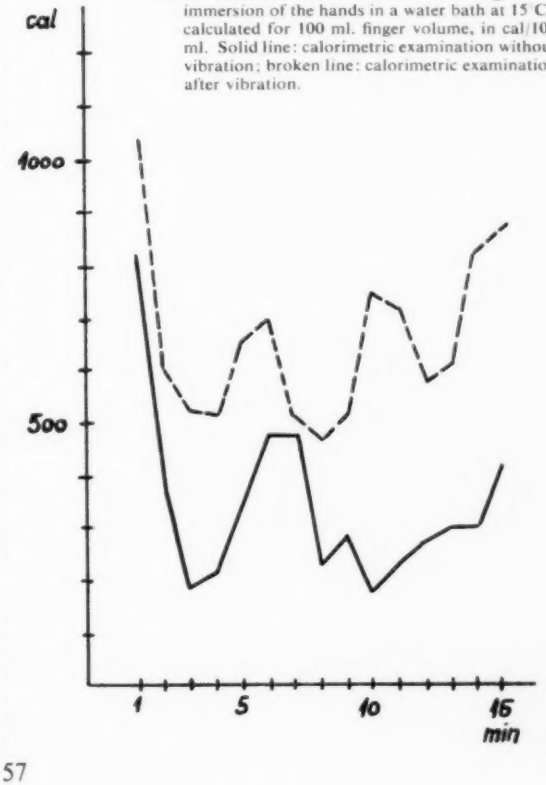

FIG. 1.—Heat elimination from the index finger after immersion of the hands in a water bath at 15° C., calculated for 100 ml. finger volume, in cal/100 ml. Solid line: calorimetric examination without vibration; broken line: calorimetric examination after vibration.

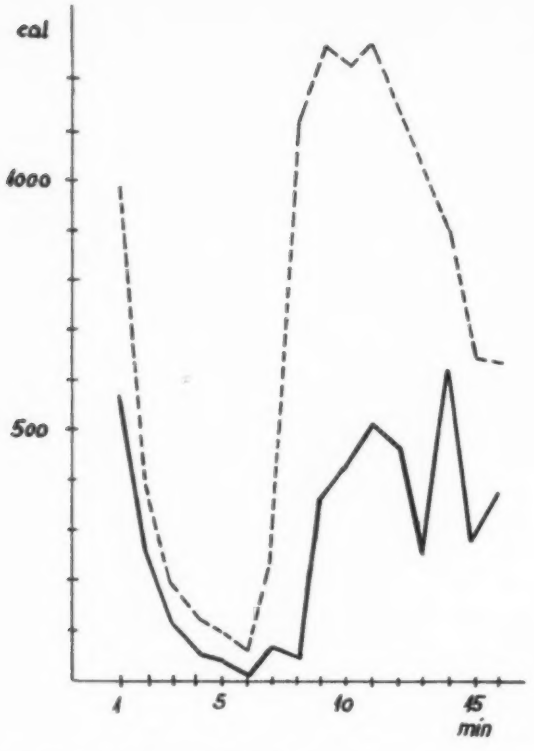

FIG. 2.—Heat elimination from the index finger, calculated for 100 ml. finger volume, in cal/100 ml. During the first six minutes the circulation was arrested. Solid line: without vibration; broken line: after vibration.

Results

It was found that the heat elimination during the initial constriction and the cold dilatation was greater after the application of vibration than before; heat elimination was greater than in the opposite (control) finger. This observation was also found when the circulation was arrested during the first six minutes. Figs. 1 and 2 show typical examples of the two experimental series.

In contrast to healthy subjects, three patients suffering from vibratory Raynaud's phenomenon gave a negative response to vibration. Their heat output both in the initial phase and the second phase of the calorimetric examination remained at a very low level.

Comments

It appears from the present study that vibration causes an increase of the internal temperature of the vibrated finger and a change in the reactivity of the blood vessels to cold (increased cold dilatation). It is likely that at the beginning of the exposure to vibration, the finger blood vessels of subjects who are not accustomed to use vibrating tools show a better defence against local cooling than those with vibratory exposure. The former react with increased cold dilatation, at least immediately after the brief vibration. Subsequently, in those who work regularly with vibrating tools, the cold dilatation decreases and the blood vessels give a negative response to vibration.

It appears from this study that the increased internal temperature of the vibrated finger is a reactive effect, as is shown by the fact that in patients suffering from Raynaud's phenomenon this effect was abolished.

It is possible that vibration stimulates the same mechanism that is responsible for the cold dilatation and that long-term repetitive stimulation causes damage to this mechanism.

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Expired Air Resuscitation in a Contaminated Atmosphere

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(RECEIVED FOR PUBLICATION JANUARY 9, 1961)

Respiratory resuscitation in an atmosphere deficient in oxygen, or heavily contaminated with poisonous substances, is a problem which may occur in some industries, and particularly in the petroleum industry. Manual methods of artificial respiration are unsuitable for obvious reasons. Either the victim has to be removed from the poisonous atmosphere before resuscitation can begin, when it may be too late, or some form of positive pressure breathing apparatus, using oxygen or compressed air, has to be employed. The latter is heavy, or may be limited in its use by the length of pipeline.

In recent years direct expired air resuscitation has been shown to be a satisfactory method of artificial respiration (Safar, Escarraga, and Elam, 1958), and it is known that this can be performed efficiently by an operator who is wearing a modified anti-gas respirator (Lucas and Whitcher, 1958). Men working in contaminated atmospheres wear some form of breathing apparatus, and modifications to a standard, open circuit, compressed air breathing set were therefore effected so that it could be used for expired air resuscitation.

Most respiratory facepieces have a plug in the side which can be used for telephonic communication. A corrugated rubber tube, 1 in. (2·5 cm.) in diameter, is inserted in place of this plug and projects into the

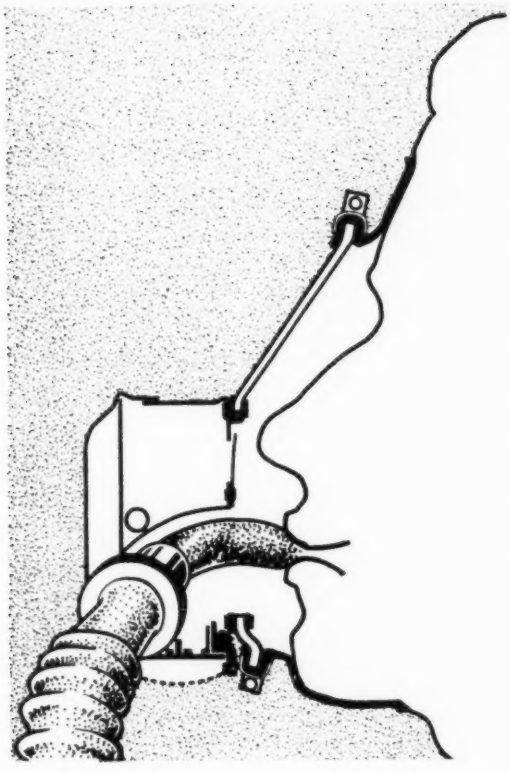

FIG. 1.—Rescue tube in position in respirator facepiece.

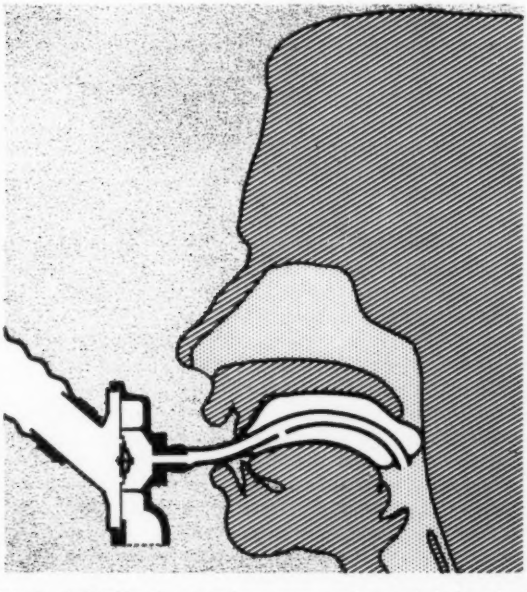

FIG. 2.—Inflatable airway and non-return valve at victim's end of rescue tubing.

facepiece so that it can be gripped by the rescuer's mouth (Fig. 1). At the other end of the tubing, which is 6 ft. 6 in. (198 cm.) long, there is a three-way inspiratory–expiratory valve such as is used on any intermittent positive pressure breathing machine. Connected to the inspiratory side of the valve is a rubber pharyngeal airway with a large self-inflatable cuff (Fig. 2). This cuff inflates on inspiration and not only makes a gas-tight seal in the pharynx, but also keeps the airway in position, so allowing the rescuer to give artificial respiration while the victim is being removed from the contaminated atmosphere.

These modifications to the facepiece are inexpensive and do not affect the ordinary use of the apparatus since the tubing need only be fitted when required. The device has been tested on a number of anaesthetized, curarized subjects and has been found to be entirely satisfactory. Fortunately, or unfortunately, it has not yet been used in an emergency.

We are grateful to J. G. Franklin and Sons Ltd., of Dalston, London, who made the inflatable airway. The complete device is now available from Siebe Gorman and Co. Ltd., of Chessington, Surrey.

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Prevention of Occupational Risks

The Third World Congress on The Prevention of Occupational Risks takes place in the Palais de Chaillot, Paris, on May 22 to 27, 1961. It is organized by the National Safety Institute of France in collaboration with the Committee on the Prevention of Occupational Risks of the International Social Security Association (I.S.S.A.) in co-operation with the International Labour Office.

The aim of the Congress is to enable international specialists to discuss various aspects of the prevention of occupational risks and to collect together the latest information on "research and progress towards prevention". This theme will be treated under three headings:

(1) The present state of research;
(2) Progress in technical fields;
(3) Progress in medical and psychological fields.

Three committees will examine these items specifically from the standpoint of the prevention of occupational risks and will discuss the latest measures for security and hygiene, new techniques and principles, and the perfection of systems which have given good results in the past.

Inquiries should be sent to the National Safety Institute, Third World Congress, 9 avenue Montaigne, Paris 8, France.

BOOK REVIEWS

Casualty Services and Their Setting: A Study in Medical Care. (Pp. viii + 135; 3 plates + 10 tables. 7*s.* 6*d.*) Published for the Nuffield Provincial Hospitals Trust by Oxford University Press. 1960.

This report derives from an assessment of casualty services in 14 areas, covered by 20 main hospitals and several smaller ones. The background landscape included fenland, mountainous moors, sea-side villages, county boroughs (some highly industrialized), and part of London town. The population in this patchwork was over five million.

The report is highly critical; critical of medical staff, accommodation, equipment, records, control of infection, and follow-up. Only the quality of the sister-in-charge scores a consistently high rating. Not a great deal is offered in the way of answers but much is offered as a guide to the questions.

A casualty department means in many places an ever-open door for one and all to enter when in need of medical treatment for sundry serious or trivial ailments or injuries at any time of the day or night. From this fact alone stem many of the valid criticisms. The department is an alternative to the general practitioner, often with extremely little communication between the overlapping medical parties concerned. Accommodation becomes overcrowded, the staff harassed with trivialities, the work unattractive to young doctors and unnoticed by consultants. An astonishing figure is given of eleven million casualty attendances during 1958—a third of all in-patient and out-patient attendances at all hospitals.

At this point a glaring weakness in records becomes apparent. Nothing is known about these cases beyond the mere number of them, the proportion that walked in on their own, or were sent by a doctor, or who arrived by ambulance is not known, nor is their age or sex or occupation, nor is anything known of their treatment and disposal. Their bare numbers are the only statistical data upon which is based such important matters as number and quality of staff. The relevant facts upon which to base a policy now and for the future are not there.

The medical staffing situation presents a gloomy picture. There is an alarming and growing shortage of junior casualty officers and on these grounds alone a strong case exists for area rationalization to ensure a reasonable cover. When senior men of S.H.M.O. grade are appointed they rarely stay long, for the post as it is at present conceived is not one to hold a high grade man. The instability of medical staffing is one of the biggest handicaps. Finally the committee criticize the lack or perfunctory nature of consultant cover. Consultant responsibility and supervision is a principle upon which hospital standards are founded but only in one of the hospitals visited did this requirement score a maximum rating.

An interesting suggestion is made (in one hospital it was already in practice) that suitable G.P.'s be appointed as casualty officers on a sessional basis, thus improving the standard of medical cover and linking the practitioners more closely with their local hospital. It is evident that a similar arrangement could be adopted with local industrial medical officers, who, in any case, are usually part-time G.P.'s.

Industrial medical services in fact operate to a large extent as extensions of the hospital casualty service. Were they to be increased, especially for small firms, where they are at present virtually non-existent, it appears likely that many of the difficulties of casualty departments in industrial towns would be solved. This is a powerful argument why the Ministry of Health should give at least some assistance to industrial health services; at present it gives none.

One of the most critical passages in the report is that dealing with control of infection and appreciation of the sepsis problem. Detailed comments on every section are given in the appendices and some of those related to cross-infection and sepsis are certainly startling but can it really be just to say that in 12 hospitals out of 18 appreciation of the sepsis problem was nil?

The report ends on the note that much confusion exists as to the function of a casualty department and little constructive thinking is being done to remedy widely known faults. While there can be no fixed pattern, a casualty service should primarily be for those injured in accidents and for medical emergencies requiring immediate attention. Each region should produce facts in order to formulate a rational policy. A great deal of field work will be required but this report has at least done much of the preliminary thinking.

T. O. GARLAND

Disc Lesions and Other Intervertebral Derangements. By E. J. Crisp. (Pp. viii + 158; 48 figures. 15*s.*) Edinburgh and London: Livingstone. 1960.

This excellent little book fills a gap for those interested in the problem of the back and its treatment, particularly by manipulation.

The first part of the book is concerned with the anatomy and physiology of the back, including its development, growth, and age changes.

Dr. Crisp's simplified interpretation of radiographs on page 23 would not be accepted by all and again his views on osteochondritis juvenalis and tight hamstrings is open to doubt. Despite these minor criticisms the greater part of this book is sound—written in a clear style and reasonably dogmatic. The *x*-ray illus-

trations are of good quality and the various diagrams explain the points well, although Fig. 17 looks very like an acute disc lesion and not due to fibrosis of the ligamenta flava—a condition rarely seen at operation.

In the section dealing with treatment all the normal methods are well described together with an excellent chapter on manipulative techniques.

This book will appeal particularly to the practitioner interested in the manipulative treatment of back disorders.

G. P. ARDEN

Evaluation of Industrial Disability, 2nd ed. By Packard Thurber. (Pp. 63; 78 figures. 10s.) New York: Oxford University Press. 1960.

This is the second edition of a book first published in 1950 by Dr. Thurber, chairman of the sub-committee for the standardization of joint measurements in industrial injury cases in California, U.S.A.

From the details and precise measurements in this book it is obvious that this subject is taken more seriously in the States than over here.

Dr. Thurber has tried to standardize the terminology, history taking, and method of measurements in industrial injury cases. A brief description is given of the normal anatomy and an attempt is made to define degrees of pain, which is almost impossible owing to the variability of patients. There are numerous photographs and diagrams showing how various parts of the spine and joints are measured. The methods closely resemble those used over here: in all cases a goniometer is used which certainly helps to reduce the margin of error.

Some confusion is caused by describing the knee and elbow range as 180° extension–140° flexion. Surely 180–40° extension range is much simpler.

What Dr. Thurber calls thumb abduction is anatomically thumb extension, abduction being at 90° to the plane of the hand. Finger movements are measured in great detail and one wonders whether functional tests would not be better, such as the power of grip and ability to hold domestic articles or tools.

At the end of the book there is a table of average joint movements and a section on eye and head injury disabilities.

This book is a laudable effort to standardize what is at the moment a somewhat inexact science, and it is particularly valuable to those doing medico-legal work and for those concerned with industrial disability examinations.

G. P. ARDEN.

Radiations in Industry: How they affect you. (Pp. 95; illustrated. 4*s*.) London: Trades Union Congress. 1960.

How does one evaluate the curate's egg, the classical example of something good in parts? Doubtless it depends on the consumer. The Trades Union Congress, who issued this booklet, must know how to judge what the average trades unionist will want to know and to write accordingly. They have not, however, been able to marry this information with scientific exactitude and so satisfy the scientific reviewer.

Chapter 1 is the plain man's guide to radiations, units, and instruments. There is too much unnecessary loose talk of "atomic radiations" and some misleading information, such as cosmic rays "are all relatively low powered" and radioactive materials enclosed "in containers . . . are then known as 'sealed sources' ".

Chapter 2 on the use of radiations in medicine, industry etc. is much better. The whole pamphlet is extremely well illustrated with photographs and this is most helpful.

Chapter 3 is on radiation risks. Here is dogma, which in the circumstances is desirable and excusable.

Chapter 4 is on safeguards. It is in most ways admirable, but marred by howlers like "the maximum genetic dose to the whole population must not exceed 5 rems per year"—an error of thirtyfold.

Chapter 5 is all about international and national ways and means, particularly committees. The most important means is education. This is one of the booklet's messages and cannot be too greatly stressed. To make this publication part of the public's educational reading would need its revision by a firm editor.

JOHN F. LOUTIT

Chemicals in Food and in Farm Produce: Their Harmful Effects. By Franklin Bicknell. (Pp. 192. 12*s*. 6*d*.) London: Faber and Faber. 1960.

In his first sentence of Chapter 12 the author writes "Congenital abnormalities, physical and mental, are mainly caused by the alien substances added to food." This provides a representative benchmark by which the well-informed medical reader can evaluate the author's knowledge and judgement. An appendix containing about 90 chemical formulae and 291 references should not lead the reader to believe that this is a scientific treatise. If he consults those references which provide factual information he might well draw conclusions sharply at variance with those drawn by the author. It is to be hoped that the credulous reader will neither die of starvation nor require the administration of tranquillizers to allay the anxiety that might be aroused by accepting this as a serious presentation of a medical problem.

J. M. BARNES

Growing Old in a Mechanized World. By F. Le Gros Clark. (Pp. 145; 3 tables. 7s. 6d.) London: The Nuffield Foundation. 1960.

This short book reviews the position of "elderly" men at work, whatever their chronological age, and comments on the trends which seem likely to take place with increasing mechanization. The problems which it highlights are widely experienced in industry, and are illustrated by a description of eight varied but fairly mechanized firms.

The book stresses the urgency of "a recasting of social values" with respect to retirement, including both financial aspects and the use people make of their

leisure. It also stimulates thought concerning present attitudes and practices to the older man at work. For example, the shortage of very "light" work for men in their 60's suggests to the reviewer that firms might find it worth while to retrain men in middle life known to be on "demanding" jobs. Mr. Le Gros Clark suspected that this was already happening informally and successfully in one of the firms.

This book should be read by all connected with the shaping of industrial policy, whether in a medical, managerial, or trade union capacity. Also, anyone interested in social problems of ageing would do well to read it and to recommend it to others.

SHEILA M. CHOWN

The Hazards to Man of Nuclear and Allied Radiations. Second Report to Medical Research Council. (Pp. 154. 7*s*.) London: H.M. Stationery Office. 1960.

The Medical Research Council, in their second report on radiation hazards, take account of recent radiobiological and genetics research work in their evaluation.

The picture is coming into better focus but remains unaltered in essentials: however, some areas of uncertainty are less blurred than in the first report in 1956.

In the Hiroshima survivors, leukaemia has been shown to have a maximum incidence in the sixth to eighth years after radiation exposure; thereafter the risk of this disease as a sequel diminishes, and there is an increased mortality from cancer, though as yet it is not possible to say whether all forms of cancer contribute to this or only certain types. Since the mean latent period for many types of cancer is more than 10 years, it is too early to say whether a peak has yet been reached in this instance.

Experimental work with mammals shows that loss of fertility is perhaps the most sensitive of all indicators of damage by irradiation and such effects, the report predicts, might be of profound biological significance under conditions of considerable over-exposure as in accidents or nuclear warfare. There is no suggestion of impaired fertility in either sex in occupational radiation exposure.

A survey of the mortality of British radiologists in a 60-year period up to 1956 shows no life-shortening effect of radiation in this group.

The views on genetic effects in the 1956 report are not materially altered. Recent experimental work shows that, in mice, fewer gene mutations are caused in spermatogonia and oocytes if a total radiation dose is spread out over a longer time than if it is given rapidly as a single brief exposure: so in this work, the effect is reduced by a lower dose-rate. This does not affect the "no-threshold" concept for genetic effects. Chromosomal abnormalities, in addition to gene mutations, may be produced by irradiation in man—hence wisdom dictates a cautious attitude at present.

According to the survey of the Adrian Committee, radiation received by the general population from diagnostic radiology is equivalent to a genetically effective dose of 14 milliroentgens (14 mr.). By comparison, the gonad dose-rate from naturally occurring radiation sources is in the range between 85 mr. and 106 mr. The reduction in gonad dose from *x*-rays used in diagnosis is praiseworthy but not yet equally good in all hospital *x*-ray departments. If the techniques of all departments could be brought up to the standard present in one-quarter of the hospitals studied, this dose could be further reduced to one-seventh of the present level, that is, about 2 milliroentgens, without any curtailment of the work.

An appendix gives additional data on fall-out from which it appears that short-lived isotopes are relatively more important than in the last report because of the changed pattern of nuclear tests. The amount of fall-out shows a seasonal trend with highest values in Spring. Distribution is non-uniform with the greatest deposition in Northern temperate latitudes. Most fall-out comes down in rain; the amounts recorded at various U.K. sampling stations are proportional to the rainfall there. Short-lived fission products are of significance in contributing to external radiation: long-lived fission products which are important are those stored in the body, strontium-90, caesium-137, and carbon-14, which give internal radiation. Strontium-90, which is concentrated in bone, is regarded as the best single indicator of possible hazard. But a sudden rapid rise in bone retention to levels higher than predicted, which was feared as a possibility in 1956, is now considered to be unlikely, so the warning level need not be quite as low as one-tenth of the permissible average population dose suggested then and is now raised to one-half.

The report concludes by repeating verbatim the views expressed in 1956 on wartime hazards and the biological significance of atomic warfare: "we have no reason to change these views".

KATHARINE WILLIAMS

Health Plans and Collective Bargaining. By Joseph W. Garbarino. (Pp. xi + 301. 40*s*.) University of California Press. 1960. (Agents in this country, London: Cambridge University Press.)

This is an important book. It appears just as the new American President focuses attention on the social services and gives a completely neutral evaluation of the parts played so far by the protagonists in the battle to decide the future of medicine in the United States.

To set the stage, the author describes how, in the past 40 years, all attempts to introduce compulsory health insurance at either Federal or State level have been defeated and how the Trade Unions, always the leaders of this movement, changed their tactics without losing sight of their original aim. Instead of beating against the door firmly closed in the face of government-sponsored health insurance, they used their collective bargaining power to force employers to introduce schemes for their employees. The inherent disadvantage of such isolated schemes in tying the employee to his employer has been outwieghed by the real need for the benefits. As a result, the number of schemes has increased with great rapidity. Some of the unions found them so lucrative that they abandoned the original idea to use the development of private schemes as a weapon with which

to coerce the medical profession as a whole. Thus the situation became increasingly complex as the medical profession, the unions (in majority and minority groups), the insurance companies, and the government all joined the fray.

Political struggles of such magnitude must be reflected in the day-to-day provision of medical care. Professor Garbarino sets out to assess this interaction and has studied the effects of the political manoeuvring on the medical services in the San Francisco Bay area of California. This area was chosen, not because it was typical of the United States as a whole, but because representative examples of all types of medical service are to be found there.

The sharp rise in the cost of medical care in the United States during the past 25 years has brought opprobrium on the medical profession. The American public cannot overlook the fact that, of all the professional men in the country, the doctors now have the highest average income. The study shows that the rise is largely due to the increase in the cost of admission to hospital, which has gone up by 319% in the time taken for the cost of living index to rise by 110%. During the same period physicians' and surgeons' fees have increased by 88% and 66% respectively. Both doctors and patients have played a part in forcing up the hospital costs, mainly by abuse of the insurance schemes. The abuses are inextricably bound up with the quality of medical care and are usually in the field of overmedication. The seriousness of this trend is revealed by the prevalence of unnecessary admission to hospital and even the performance of unnecessary operations.

The reaction of the American medical profession to various political pressures has been the subject of study first, at the level of the American Medical Association, next, at the level of the State or County Medical Society (which is all-powerful in the control of the methods of medical practice) and finally at the level of the individual practitioner. The arguments for Federal and for State medical plans are elaborated and the plans themselves are compared with the group practice pre-payment schemes organized by practitioners, and with the services provided by insurance companies.

The effect of these developments on the movement towards compulsory health insurance on a national basis is evaluated and the book ends with the conclusion that the growth of private health insurance, and in particular of collectively bargained plans, has virtually eliminated the possibility of a governmental monopoly of health insurance in America.

Professor Garbarino is an economist with a special interest in industrial relations. He has presented us with a most topical evaluation of a situation that Mr. Kennedy will find hard to unravel.

C. J. H. MANN

Morbidity Statistics from General Practice. Volume II (Occupation). By W. P. D. Logan. (Pp. vii + 269. 25*s*.) London: H.M.S.O. 1960.

This is the second volume presenting the results of a statistical study of some 280,000 clinical records of over 100 general practitioners in England and Wales from May 1955 to April 1956, carried out jointly by the College of General Practitioners and the General Register Office. The amount of sickness for which patients consulted their doctors and its distribution by sex, age, and area was described in the first volume. This volume deals with its distribution by occupation and is based on the records from 76 practices which had on their lists 85,352 males and 96,727 females aged 15-64, and 58,427 children. Only patients on National Health Service lists were included so that data about occupational groups likely to be private patients must be incomplete.

The measurements of morbidity that have been used are the consultation rate (number of consultations recorded in 12 months/1,000 patients on lists) and the patient consulting rate (number of patients who had one or more consultations in 12 months/1,000 patients on lists) with the emphasis on the more useful latter index.

Because the occupational description of each individual was obtained from only one source (the doctor's record card) the occupational classification in this study does not contain one of the major sources of error of the studies of occupational mortality—the collection of information about occupation from different sources, the numerator from death registration records, and the denominator from the Census. However, information about occupation in this study was obtained by the general practitioners asking the patients the nature of the work performed and the article or commodity made or dealt in or the material worked in. There seem to be risks of considerable inaccuracy here. One-third of the patients included in the survey did not consult their doctors and for these information about their occupation was obtained from any other member of the family who had a consultation during the year. The Classification of Occupations used in the study was the one used for the 1951 Census of Occupations. There were small numbers of patients in some occupational categories which curtailed the amount of tabulation possible, and the reader is warned that many of the figures in the tables may have a large element of uncertainty due to the possibility of chance fluctuation.

The age structure of the population at risk was available from the general practitioners' records but it was not possible to carry out extensive age-standardization. A series of standardized patient consulting ratios for men analogous to standardized mortality ratios is presented but it is not clear how far the age standardization goes within the age-range 15-64.

With the reservations mentioned, and there are reservations with all morbidity data, there is a wealth of interesting material in the 160 pages of tables. There are consultation and patient consulting rates for men aged 15-64 by diagnoses and by occupational groups, social classes, and socio-economic groups for retired men, for men aged 65 and over, for women aged 15-64 (those in whole time and part time occupation and housewives), and for children classified by fathers' occupations. There are some interesting social class gradients in some diagnoses which are commented upon in the text.

The study is complementary to those from individual

industries, from the Ministry of Pensions and National Insurance, hospitals, and the Survey of Sickness. It will be interesting to compare the data with those from the forthcoming sample survey of sickness absence by occupation to be undertaken by the Ministry of Pensions and National Insurance.

P. A. B. RAFFLE

BOOKS RECEIVED

Review in a later issue is not precluded by notice here of books recently received.)

Bericht Über Das Gesundheitswesen in Österreich im Jahr 1959. (Pp. 203; illustrated. S 50.-.) Bundesministerium für soziale Verwaltung, in conjunction with Österreichischen Statistischen Zentralamt. 1960.

First Aid in the Factory. By Lord Taylor, with the assistance of W. N. Booth, B. S. Laing, and O. Ross, with a Foreword by A. Austin Eagger. (Pp. x + 140; 72 figures. 9*s.* 6*d.*) London: Longmans, Green. 1960.

Pneumoconiosis in the Mining and Quarrying Industries. Digest of Statistics 1959. (Pp. iv + 19; 15 figures. 3*s.* 6*d.*) London: H.M.S.O.

The Nuffield Foundation, Fifteenth Report. Report for the Year ended March 31, 1960. (Pp. xiii + 144.) London: The Nuffield Foundation. 1960.

L'Automation. Aspects Psychologiques et Sociaux. By A. Chaparis, A. Lucas, E. H. Jacobson, N. H. Mackworth, L. Ancona, and G. Iacono. (Pp. 119; 10 figures. 110 PB.) Louvain: Éditions Nauwelaerts. 1960.

Department of Industrial Health, Tata Services Private Limited. Annual Report, 1959. (Pp. 24; 9 tables.) Bombay: Tata Services Private Limited. 1960.

Modern Occupational Medicine, 2nd ed. Edited by A. J. Fleming and C. A. D'Alonzo. Associate Editor—J. A. Zapp. (Pp. 587; 66 figures + 1 coloured plate. 90*s.*) London: Henry Kimpton. 1960.

Occupational Health Review, Vol. 13, No. 1. (Pp. 26; 6 figures + 2 tables.) Ottawa: Occupational Health Division, Department of National Health and Welfare. 1961.

Air Pollution. With various contributors. (Pp. 442; illustrated. 40*s.*) Geneva: World Health Organization. 1961.

Micro-organisms as Allies. By C. L. Duddington. (Pp. 256; 21 figures. 25*s.*) London: Faber and Faber. 1961.

Medical Forms and Procedures for Industry. By Herbert L. Herschensohn. (Pp. xv + 192. 68*s.*) Springfield, Illinois: Charles C. Thomas; Oxford: Blackwell Scientific Publications. 1961.

Better Offices. Foreword by Prof. Sir William Holford. (Pp. 180; illustrated. 12*s.*) London: Institute of Directors. 1961.

A New Academic Course in Occupational Hygiene

With the aid of a grant of £20,000 from the Nuffield Foundation the London School of Hygiene and Tropical Medicine is offering a new course in occupational hygiene. It will be whole time for nine months starting on October 2, 1961. The course is open to graduates whose undergraduate studies, or previous experience, provide a suitable preliminary training. In general, graduates in physics, chemistry, engineering, medicine, or allied subjects would have the necessary background. In special circumstances non-graduates would be accepted.

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3. *Epidemiology and statistics:* the purpose and methods of epidemiology used in field and laboratory studies.

4. *Physiology, occupational toxicology, and disease:* elementary principles of physiology and toxicology and descriptions of occupational injuries and diseases.

5. *Information and reports:* sources of information and uses of libraries, the presentation of technical reports and scientific papers.

Practical instruction will be a major feature of the course and will comprise demonstrations, exercises in environmental measurements, and visits to factories and other places and institutions.

The grant from the Nuffield Foundation will be used to equip a teaching laboratory and to offer a training fellowship for a graduate to take this course with the prospect of appointment to the staff of the Department of Occupational Health at the London School of Hygiene and Tropical Medicine at the end of the course.

Further particulars on qualifications for admission and fees may be obtained from the Registrar of the London School of Hygiene and Tropical Medicine, London, W.C.1.

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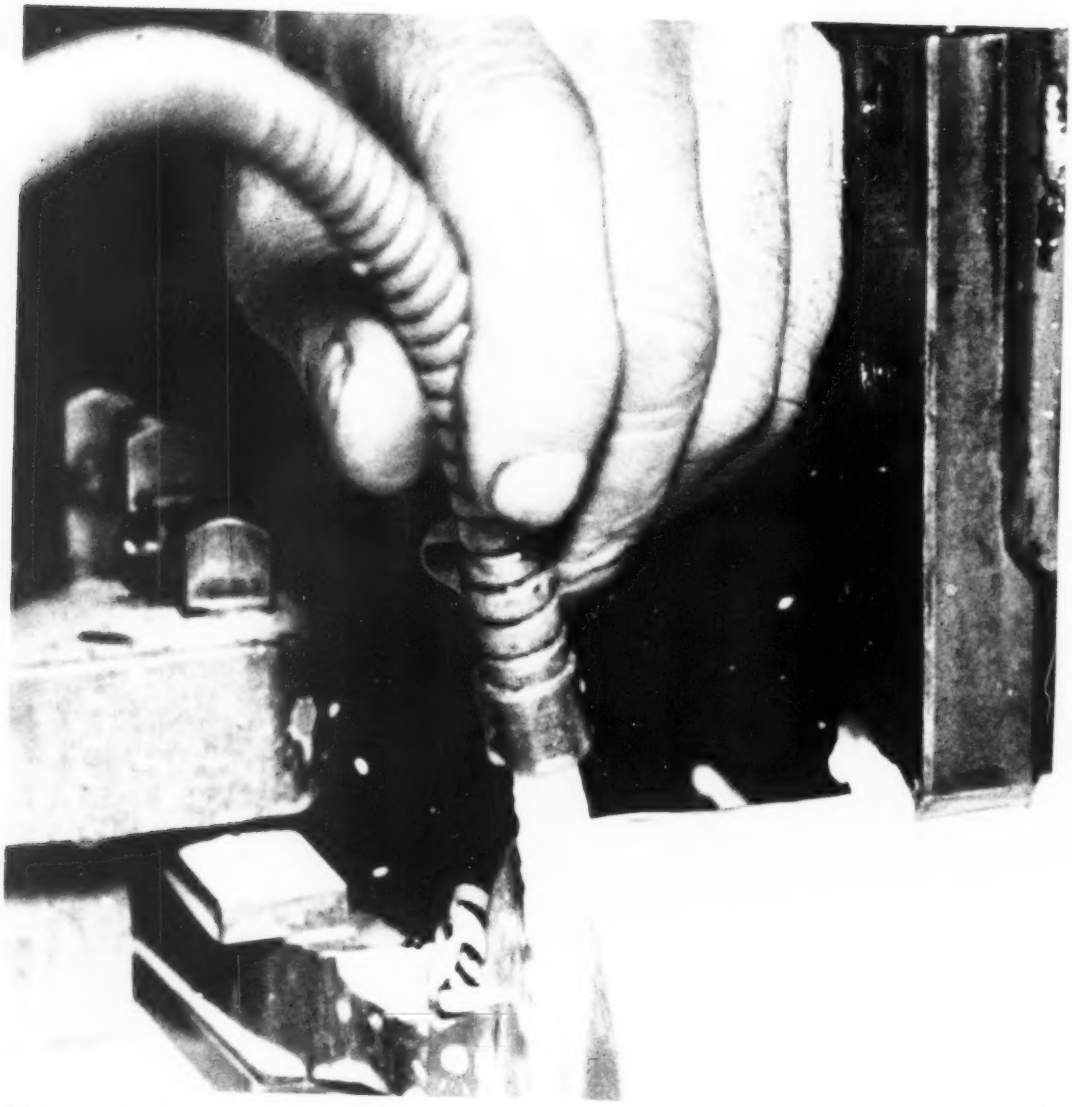

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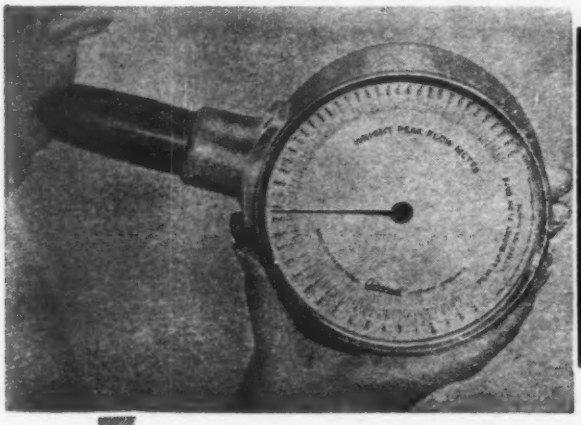

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